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The Relation Between the Results of ABO and Rh Tests and the Clinical Condition of 2,000 Mothers and Infants

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IN the early months of 1944 we planned a blood-group investigation of 2,000 consecutive cases of women booking for delivery at St. Helier County Hospital. It was felt that from such a series information, referable to both baby and mother, could be obtained which would not be forthcoming from a serological study of only those families in which haemolytic disease of the foetus (erythroblastosis foetalis) had occurred. The condition of (*a*) the baby, and (*b*) the mother, was investigated under the following headings.

THE CONDITION OF THE BABY.

(1) The frequency of haemolytic disease of the foetus or newborn.

(2) The possibility of the association of a normal infant with the presence of anti-Rh or other atypical agglutinins in the maternal serum incompatible with the infant's erythrocytes.

(3) The possible relation between "physiological" jaundice and blood-group incompatibilities between the mother and infant.

(4) The possibility of a serological reason for some of the miscarriages and stillbirths usually relegated to the category "cause unknown."

(5) The relation between parity and the above clinical conditions of the infant.

THE CONDITION OF THE MOTHER.

(1) The proportion of Rh negative women with Rh positive infants who form Rh antibodies.

(2) The time at which Rh agglutinins are first detectable in the maternal serum during pregnancy.

(3) The possible association of pre-eclamptic toxaemia of pregnancy and eclampsia with a blood-group incompatibility between mother and foetus.

At the time this investigation was started no large unselected series of cases had been reported. Later Broman (1944) reported the results on 914 random mothers and babies. He found 3 cases of haemolytic disease of the foetus among these. In each case the mother was Rh negative, the infant Rh positive and the maternal serum contained Rh antibodies. He did not find anti-Rh agglutinins in the sera of mothers of normal children or of children showing physiological jaundice. He concluded that there was no connexion between the latter condition and icterus gravis. He also investigated toxaemia of the mother in relation to her ABO group and Rh type, but could not find a connexion. Belson (1946) reported that among 300 unselected pregnancies there was 1 proven case of haemolytic disease and 2 cases in which the infant was mildly jaundiced. The mothers of both these latter infants were Rh negative and the serum of one of them contained Rh agglutinins.

Harrison and Meacock (1945) have reported 280 cases which were referred to them for Rh blood-type investigation. Their series included cases where the infant was stillborn, had a congenital abnormality, suffered from haemorrhagic disease of the newborn, or haemolytic disease of the foetus, or died in the neonatal period from conditions other than haemolytic disease of the foetus or where the mother had toxaemia of pregnancy or repeated abortions. They found no connexion between these conditions and Rh incompatibility, except in the case of haemolytic disease of the foetus.

On the other hand, Javert (1942) found that in 16 cases of hydrops foetalis 5 of the mothers had toxaemia of pregnancy. Schumann and Levine in 1946, reporting a 62 per cent toxaemia-rate in the mothers of infants suffering from erythroblastosis foetalis, stated that it was highest when the infant was hydropic. In a series of 13 cases (7 proved haemolytic disease and 6 probable) Schwartz and Levine (1943) found 9 instances of toxaemia of pregnancy in the mother and they suggested that the toxaemia might be due to foetal blood being agglutinated in the maternal circulation. They felt that further investigation was necessary.

Halbrecht (1944) studied 60 cases in which icterus appeared within 24 hours of birth, but was not associated with other clinical signs. He gave to this form of icterus the name icterus praecox to distinguish it from icterus gravis and physiological icterus. As in 57 of the 60 cases (95 per cent) the infant's red cells were incompatible with the mother's serum according to ABO blood grouping, he concluded that these incompatibilities played some part in the aetiology of icterus praecox. He also found that of 160 cases of jaundice, appearing more than 24 hours after birth (physiological jaundice) only 48 infants (30 per cent) had red cells incompatible with the mother's serum. In a control series of 2,000 unjaundiced infants the incidence of such incompatibility was 26.5 per cent. Wiener (1946), in a series of 42 cases in which jaundice was noted by the clinicians in the first or second day after birth, found that 81 per cent of the infants had red cells which were incompatible with their mothers' sera according to ABO grouping.

Technical Methods.

Blood Samples.

Samples of maternal blood were obtained from a superficial vein. Samples of infant's blood were obtained from the cord. A 2 per cent suspension of the red cells from

the clot was used for grouping and Rh typing. The maternal serum free from red cells was examined for antibodies.

ABO Grouping.

This was performed by the tube technique as described by Taylor, Race, Prior, and Ikin (1942) in which both red cells and serum are tested.

Rh Typing.

The technique was essentially similar to that for ABO grouping except that the tubes were incubated at 37°C. and great care was taken in the reading to avoid breaking up the agglutinates (Boorman, Dodd, and Mollison, 1942). In the early stages of the investigation the samples were tested with 4 anti-Rh sera (2 anti-D, 1 anti-D + anti-C and 1anti-E); later the anti-E was omitted owing to shortage of serum, and for the last part of the series all samples were tested with a single high titre anti-D serum and those which were negative were then retested with sera containing anti-C and anti-E to detect the R′ (Cde) and R″ (cdE) red cells. However, in the tables the 15 R′ and 7 R″ women found are included among the Rh negatives as they are equally capable of forming anti-Rh agglutinins (Anti-D).

Detection of Rh Antibodies.

The serum from each woman was tested at 37°C. against standard red cells of types R_1R_1 (CDe CDe) R_2R_2 (cDE cDE) and rr (cde cde) in order to detect, and differentiate between, the 6 Rh antibodies, i.e., anti-C, anti-D, anti-E, anti-c, anti-d, and anti-e.

Titration of Antibodies.

The technique for titration of antibodies was that in routine use in this laboratory (Boorman, Dodd and Mollison, 1945) in which serial dilutions of the serum are incubated with standard cells. ABO titrations are kept at room temperature and Rh titrations at 37°C. The titre of the serum is expressed as the reciprocal of the greatest dilution causing agglutination (an even distribution of clumps of 3 or more cells was accepted as evidence of agglutination.

Coombs Test.

(*a*) *Indirect test.* This test was first described by Coombs, Mourant and Race (1945) for the detection of Rh antibodies, especially the incomplete or blocking antibody. The serum to be tested is incubated with standard red cells as for the direct agglutination test. The supernatant serum is then removed and the red cells carefully washed 3 times in a large volume of normal saline. Anti-human-globulin (prepared in a rabbit) is added to the washed cells and the mixture is allowed to stand for at least ¾ hour at room temperature. Since the rabbit serum is anti-globulin, a clumping of the red cells indicates that an antibody-globulin has become attached to them.

(*b*) *Direct Test.* The direct Coombs test is used for the detection of cells sensitized by an antibody *in vivo*. The red cells to be tested are freed from serum by washing 3 times in a large volume of saline. A 2 to 5 per cent suspension in saline is then prepared. One volume of this suspension is incubated at room temperature from ¾ hour to 1 hour. A clumping of the cells indicates that they have an antibody attached to them.

After August 1945, therefore, we used these tests in cases in which the clinical diagnosis was in doubt and in which no antibody could be detected by the ordinary iso-agglutination technique to detect any antibodies which might be present in the maternal serum or any sensitization of the infant's red cells.

Serological Investigations

A blood sample was taken from every case, at the first visit to the antenatal clinic: this was usually at about the 12th week of

pregnancy, but in a few instances was much later.

The ABO group and Rh type were determined and the serum examined for atypical antibodies. Where antibodies were present, these were titrated at monthly intervals until the 34th week of pregnancy and then each week until delivery and again at the 10th day of the puerperium. Where the mother was Rh negative and without anti-Rh agglutinins in her serum or, if Rh Positive, gave a history of unexplained miscarriages or stillbirths, samples were tested at the 34th week of pregnancy, at delivery and at the 10th day of the puerperium. All other cases were retested at delivery only. The ABO group and Rh type of the infant were determined from the cord blood and the infant's red cells were tested against the mother's serum at 37°C. to detect any incompatibility.

Clinical Criteria.

Haemolytic disease of the foetus and newborn. Each case of haemolytic disease was diagnosed by taking into account both clinical and serological findings. The clinical syndromes included under this heading were:—

(1) Hydrops foetalis.

* (2) "Stillbirth" without hydrops, in the absence of any other obvious cause in cases where the mother's serum contained an atypical antibody incompatible with the infant's red cells.

(3) Icterus gravis.

(4) Congenital anaemia of the newborn.

For more detailed diagnostic criteria see Boorman, Dodd and Mollison (1944).

* In point of fact there was no case in our series fulfilling these criteria although there were 3 cases (see below) in which the infant was stillborn and the mother's serum contained anti-Rh agglutinins, but they are not considered proven cases of haemolytic disease as we were unable to test the infant's erythrocytes.

Physiological Jaundice.

The cases in this group were reported to us by several different observers and therefore we had to adopt definite criteria. These were that the jaundice should be well marked, transient and develop on or after the second day of life. Three cases where the jaundice developed as early as the first day are also included as there were no other clinical or serological indications for the diagnosis of icterus gravis and the jaundice cleared within 10 days of delivery. The ruling that the jaundice should be well marked no doubt accounts for the small number of cases of physiological jaundice found in the series as the very mild cases are thus excluded.

Stillbirths and Miscarriages.

In accordance with the usual practice we have regarded a foetus dying before the 28th week of pregnancy as a "miscarriage" and after the 28th week as a "stillbirth."

Toxaemia of Pregnancy.

We have followed here for purposes of comparison the standard finally adopted in the People's League of Health Experiment (People's League of Health 1942) and have classed as toxaemic those women with albuminuria with or without, but almost invariably with, hypertension and oedema. Those cases in which there was transient mild albuminuria associated with a urinary tract infection were excluded.

Selection of Cases.

We have called this an unselected series but there are obvious fallacies in applying this term to women booking for hospital confinement when shortage of accommodation entails strict assessment of the need for admission to hospital in each case. We were able to accept a high proportion of the primigravidae who applied in early preg-

nancy, but we booked parous women only if they had had previous obstetric difficulty or some associated disease, or if their circumstances made domiciliary delivery impracticable. This last group, however, is reasonably large and to a very great extent balances those accepted for obstetric abnormalities.

A full statistical survey of the material is being made and will be published elsewhere. However, there was no selection in favour of any of the ABO groups or Rh types as the distribution was almost exactly that expected for a random English population (see Tables I and II). The selection in favour of primigravidae was approximately 10 per cent compared with the Registrar General's figures for primigravidae in this area in 1944. The cases were not selected with any regard to their serological picture with the exception of 2 where there was known to be Rh-sensitization due to a previous pregnancy in which the infant was affected with haemolytic disease.

A follow-up was made of 241 of the women who, having attended the antenatal clinic were for various reasons delivered elsewhere. This was to determine whether we were missing any miscarriages and stillbirths because they were not being delivered in the hospital. There were 14 such miscarriages and 7 such stillbirths. This was greater than the proportion found in the 2,000 cases delivered in the hospital and therefore an attempt was made to determine whether they were due to ABO or Rh incompatibilities. Of the 14 women who miscarried, 13 were Rh positive and one Rh negative; this means in all probability that Rh antibodies would not be present in more than 1 of these cases. Nine of the women were group A, 4 were group O, and 1 was group AB; thus it is most likely that in only a few of them there would have been an ABO incompatibility between mother and foetus. Of the 7 women whose infants were stillborn all were Rh positive and therefore an Rh incompatibility is unlikely; 5 were group A and 2 group O, and therefore it is to be expected that the foetus would have been compatible with the maternal serum in the majority of these cases. We feel that it is unlikely that many of these stillbirths and miscarriages were, in fact, due to either Rh or ABO incompatibilities between mother and foetus.

The Condition of the Baby.

(1) *The frequency of haemolytic disease of the foetus or newborn.*

The percentage occurrence of haemolytic disease of the foetus in the whole series was 0.60 (12 in 2,000) which is higher than that formerly quoted—0.25 by Javert, 1937—and that found by Broman (1944) but is in accord with the estimate of its frequency now held by most of the workers in this field both in England and the United States of America. Moreover there were 7 infants (3 stillborn and 4 diagnosed as physiological jaundice), where there was an atypical antibody in the maternal serum, who might have been more properly diagnosed as suffering from haemolytic disease. The inclusion of these cases would bring the percentage occurrence of the disease to the very high figure of 0.95 per cent.

The distribution of haemolytic disease of the infant among the various ABO groups of the mother was not significant although the incidence was slightly higher where the mother's blood group was A or AB than where the mother was group O or B (Table II). There was, however, a decided preponderance of haemolytic disease of the foetus where the mother was Rh negative (Table I). In only 1 case of haemolytic disease was the mother Rh positive, and there was an agglutinin of the rhesus type anti-c present.

The following are short case notes of the cases of haemolytic disease of the foetus.

201. K. B., aged 33, 4-gravidae, group O, Rh negative. First pregnancy was normal but in the second and third there was foetal death shortly before term. Postmortem examination of the third child had shown erythroblastosis. The 4th pregnancy progressed normally until the 26th week when, after considerable uterine haemorrhage, for which the woman was transfused, she was delivered of a dead foetus showing signs of hydrops foetalis. The foetus was O, Rh positive and the maternal serum contained Rh antibodies, titre 128.

393. D. R., aged 33, 2-gravidae, group A, Rh negative. First pregnancy was normal but the woman received 2 transfusions (Rh type unknown) during the puerperium. Surgical induction was performed at the 39th week of the second pregnancy because of the presence in her serum of and Rh antibody (titre 2). A 6 pounds 10 ounces baby (group O, Rh positive) was delivered in good condition but became jaundiced a few hours later. He was transfused with 250 ml. of Rh negative blood during the first day; this raised the haemoglobin to 144 per cent. The following day he became oedematous and showed neck rigidity. Death occurred on the fourth day and postmortem examination confirmed kernicterus.

610. J. P., aged 36, 5-gravidae, group A, Rh negative. The first baby was normal, the second died of " obstructive jaundice " (in 1939). The third pregnancy resulted in a 3 months' miscarriage. The fourth pregnancy was normal but the baby (A, Rh positive) developed jaundice soon after delivery (see case report below). The antibody-titre was 8 early in the fifth pregnancy and rose to 64 at 37 weeks. The membranes were accordingly ruptured artificially and a few hours later a baby weighing 6 pounds 12 ounces was delivered, pale but lusty (group O, Rh positive). An immediate transfusion of 200 ml. of Rh negative blood was given through the umbilical vein. Jaundice developed within a few hours and the following day twitch-

TABLE Ia.

Details of Present Child in 2,000 Families Divided According to Rh Type of Mother.

Blood type of mother		Clinical condition of infant: Normal	Stillbirth	Miscarriage	Physiological jaundice	Haemolytic disease	Total
Rh negative	Number	292	6	5	22	11	336
	Per cent	86.9	1.8	1.5	6.5	3.3	16.8
Rh positive	Number	1556	14	9	84	1	1664
	Per cent	93.6	0.8	0.5	5.0	0.1	83.2
Total	Number	1848	20	14	106	12	2000
	Per cent	92.4	1.0	0.7	5.3	0.6	100.0

TABLE Ib.

Details of all the Children in 2,000 Families.

Blood type of mother		Clinical condition of infant: Normal and physiological jaundice*	Stillbirth	Miscarriage	Haemolytic disease	Total
Rh negative	Number	539	26	63	20	648
	Per cent	83.2	4.0	9.7	3.1	17.4
Rh positive	Number	2738	67	260	1	3066
	Per cent	89.4	2.1	8.5	<0.1	82.6
Total	Number	3277	93	323	21	3714
	Per cent	88.2	2.5	8.7	0.6	100.0

* No attempt was made to assess the number of previous children who had suffered from physiological jaundice as it was felt that the evidence would be unreliable.

ing was noticed. Death occurred on the third day, postmortem examination showing extreme kernicterus. The titre of Rh antibodies in the maternal serum rose to 1,000 after delivery.

685. M. P., aged 35, 3-gravidae, group O, Rh negative, had a normal pregnancy followed by an abortion at 24 weeks, the foetus being macerated. The 3rd pregnancy was normal except for a rising titre of Rh antibodies at the 37th week. Surgical induction was performed on this account and resulted in a 6 pounds baby (Group O, Rh positive) being delivered slightly asphyxiated after a normal labour. An hour after birth 150 ml. of Rh negative blood was transfused into a saphenous vein. The baby did not become jaundiced and the haemoglobin on the 6th day was 110 per cent. She was discharged with the mother on the 11th day in good condition and was seen weekly by the paediatrician. In the fourth week she appeared to be very well but the haemoglobin had fallen to 46 per cent and she was therefore given a transfusion of 200 ml. of Rh negative blood. This raised the haemoglobin level to 84 per cent and thereafter progress was satisfactory. The titre of Rh antibodies in the maternal serum was 256.

1372. M. M., aged 35, 3-gravidae, group A, Rh negative, had had a normal baby followed by an early abortion. Pregnancy and labour were normal but the group O, Rh positive baby weighing 7 pounds 5 ounces was seen to be jaundiced 8 hours after birth, when the haemoglobin was 96 per cent. Jerky movements of the limbs were noted on the second day. On the fifth day 150 ml. of Rh negative blood were given as the haemoglobin had fallen to 54 per cent. During the next 10 days the level did not fall below 84 per cent but thereafter there

TABLE IIa.

Details of Present Child in 2,000 Families Divided According to the ABO Group of Mother.

Blood type of mother		Clinical condition of infant					
		Normal	Stillbirth	Miscarriage	Physiological jaundice	Haemolytic disease	Total
O	Number	820	9	6	55	2	892
	Per cent	91.9	1.0	0.7	6.2	0.2	44.6
A	Number	812	9	6	38	8	873
	Per cent	93.0	1.0	0.7	4.4	0.9	43.65
B	Number	155	2		10	1	168
	Per cent	92.2	1.2		6.0	0.6	8.4
AB	Number	61		2	3	1	67
	Per cent	91.0		3.0	4.5	1.5	3.35
Total	Number	1848	20	14	106	13	2000
	Per cent	92.4	1.0	0.7	5.3	0.6	100.0

TABLE IIb.

Details of all the Children in 2,000 Families.

Blood type of mother		Clinical condition of infant				
		Normal and physiological jaundice	Stillbirth	Miscarriage	Haemolytic disease	Total
O	Number	1450	36	139	3	1628
	Per cent	89.1	2.2	8.5	0.2	43.9
A	Number	1430	41	141	15	1627
	Per cent	87.8	2.5	8.7	1.0	43.9
B	Number	292	12	32	1	337
	Per cent	86.8	3.4	9.5	0.3	9.0
AB	Number	105	4	11	2	122
	Per cent	86.0	3.3	9.0	1.7	3.2
Total	Number	3277	93	323	21	3714
	Per cent	88.2	2.5	8.7	0.6	100.0

was a drop to 70 per cent. The baby progressed well with iron. The Rh antibody-titre rose to 1,000 after delivery.

1521. J. P., aged 24, 4-gravidae, group O, Rh negative, had had 3 normal pregnancies. The fourth pregnancy resulted in a living infant weighing 7 pounds (group O, positive) a week after term. He was never jaundiced but became progressively paler until the 12th day when the haemoglobin had fallen to 50 per cent. He was then transfused with 200 ml. of Rh negative blood with satisfactory result, in that 2 weeks later the haemoglobin was 82 per cent. The child was given iron for a considerable time and did well. The titre of anti-Rh agglutinins in the maternal serum was 2.

1573. E. H., aged 32, 4-gravidae, group A, Rh negative. The first infant was normal. The second was stillborn (cause unknown) and the 3rd was diagnosed as a case of marasmus when 3 weeks old and was in hospital for 7 months but eventually did well. The fourth pregnancy was complicated by pyelitis associated with pathological hydronephrosis. Artificial rupture of the membranes was carried out shortly before term. The foetal heart slowed to 90 beats per minute in early labour but the baby, weighing 6 pounds 11 ounces (group A, Rh positive), cried soon after spontaneous delivery. Slight jaundice was noticed at once and the haemoglobin was only 40 per cent. Rh negative blood, 200 ml., was given a few hours later and the following day the haemoglobin was 100 per cent. This level was maintained until the end of the third week when it had fallen to 80 per cent. The child was followed up by the paediatrician and progressed satisfactorily without further treatment. In this case the titre of anti-Rh agglutinins was 2.

1625. E. N., aged 36, 7-gravida, group AB, Rh negative. This woman's first pregnancy ended by miscarriage: the second produced a stillborn infant after a breech delivery. She had then 3 normal infants. The sixth pregnancy resulted in a baby dying of kernicterus. At the 37th week of the seventh pregnancy surgical induction for a rising incomplete antibody-titre was performed. The infant, weighing 5 pounds 8 ounces (group A, Rh positive), was satisfactory at birth. However, the Coombs test done on the cord blood was positive. The following day there was a very mild jaundice. The haemoglobin was 118 per cent but there was no erythroblastaemia. The next day the jaundice was deeper and the child was irritable. Haemoglobin 108 per cent. Death occurred on the fourth day from kernicterus proved by autopsy. There were no complete anti-Rh agglutinins in the maternal serum but a strong incomplete or " blocking " Rh antibody—titre 128 by the Coombs technique.

2005. J. P., aged 32, 7-gravidae, group A, Rh negative, had only 3 living children. The third, fourth, and sixth had died of jaundice within a few days of birth. Labour was induced surgically at 38 weeks for a rise in Rh antibody-titre. The 12 pounds 13 ounces baby (group O, Rh positive) was lusty at birth and did not become jaundiced until the following day. On the third day she became drowsy and had grunting respirations and death took place the next day. The haemoglobin level did not fall below 90 per cent and, therefore, transfusion was not given. Postmortem examination confirmed the diagnosis of kernicterus with erythroblastosis. The titre of the anti-Rh agglutinins in the maternal serum after delivery was 64.

2181. G. Y., aged 33, 4-gravidae, group A, Rh negative, had a normal first pregnancy, followed by an early abortion. The third pregnancy was an ectopic gestation resulting in a tubal mole. Curiously enough, this was removed early in her fourth pregnancy before she had missed a period. A baby weighing 6 pounds 5 ounces (group O, Rh positive) was delivered normally at term in good condition but covered with yellow vernix. The haemoglobin was then 112 per cent but had fallen to 93 per cent on the following day when the baby was deeply jaundiced. A blood transfusion of 200 ml. on the third day raised the haemoglobin level to 118 per cent but the child was obviously ill and the limbs were becoming spastic. Death on the fourth day was due to kernicterus, confirmed by post-mortem examination. The titre of the maternal Rh antibodies was 256 after delivery.

2560. A. A., aged 34, 3-gravidae, group B, Rh negative, had 2 normal children. The third infant, group O, Rh positive, weighing 6 pounds 2 ounces was delivered spontaneously at 38 weeks but showed mild asphyxial signs. Jaundice was first apparent on the third day and never severe. The haemoglobin, however, steadily fell from 114 per cent to 80 per cent from the 5th to the 9th day. A level of 70 to 80 per cent was thereafter main-

tained in hospital and follow-up showed rapid improvement. This was a case where the icterus might well have been regarded as physiological, but, as the maternal serum contained an anti-Rh agglutinin (titre 64), it was diagnosed as a mild case of haemolytic disease of the foetus, especially as the baby's washed cells gave a positive Coombs' reaction.

563. A. M., aged 29, 2-gravidae, group A, Rh positive (R_1R_1 CDe CDe). The first pregnancy and labour were normal but she received a transfusion (Rh type unknown) during the puerperium for anaemia associated with sepsis. The 2nd pregnancy was uneventful and resulted in a 6 pounds 15 ounces infant, delivered normally, at term. The following day he was jaundiced and this became very marked on the third day but the haemoglobin did not fall below 112 per cent and there was no evidence of erythroblastaemia. He was discharged free from jaundice on the 11th day, but subsequently developed mild anaemia. The infant was group A, Rh positive (R_1r or CDe cde) and the mother had anti-c (anti-St or anti-Hr) in her serum (titre 8).

The following are notes on 4 cases of haemolytic disease which occurred in the hospital just prior to the present series.

1. N. M., aged 29, 5-gravidae, group A, Rh negative; had 3 normal children followed by a miscarriage at 2 months. The fifth pregnancy resulted in the premature delivery at 36 weeks of twins, 1 macerated (maturity about 18 weeks) The living twin (A, Rh positive), weight 4 pounds 6 ounces, showed evidence of haemolytic disease and died on the fourth day with marked kernicterus. The titre of the anti-Rh agglutinin in the maternal serum was 64.

2. V. M., aged 28, 4-gravidae, group O, Rh negative. The first infant was normal but the pregnancy was complicated by toxaemia and there was a postpartum haemorrhage. The second and third children were stillborn at term. Labour was induced at the 37th week of the 4th pregnancy because of the presence of anti-Rh agglutinins and the history of stillbirths. A 5 pounds 9½ ounces live child (group A, Rh positive), resulted. She became jaundiced 19 hours after delivery and was transfused on the second day. Death occurred on the fourth day, postmortem examination confirming the diagnosis of kernicterus. The titre of the anti-Rh agglutinin in the maternal serum was 8.

3. E. N., aged 35, 6-gravidae, group AB, Rh negative. This was the sixth pregnancy of the woman whose seventh pregnancy is described above (No. 1625). The baby weighed 6 pounds 12 ounces, was group B, Rh positive, and became jaundiced soon after birth, dying on the fourth day with kernicterus. Rh agglutinins titre 2 were present in the maternal serum.

4. J. P., aged 35, 4-gravidae, group A, Rh negative. This was the fourth pregnancy of a woman described above (No. 610). The baby weighed 6 pounds 4 ounces, was delivered spontaneously at the 38th week (group A Rh positive), and became jaundiced soon after birth. She was given 3 transfusions during the next 10 days and was discharged progressing satisfactorily. She was readmitted at 4 weeks in extremis due to umbilical haemorrhage and died in spite of transfusion. The titre of Rh antibodies in the maternal serum rose to 512 after delivery.

Of the 17 infants affected with haemolytic disease of the foetus (12 in the series) 2 were stillborn, 9 died in the neonatal period, and 6 survived. All but 1 of these infants who died in the neonatal period showed evidence of kernicterus. There seems to be no obvious reason why approximately 50 per cent of the affected infants developed kernicterus, but this accounts for the fact that, in spite of supervision and treatment, the percentage of affected infants surviving was only 35 per cent.

(2) *The possibility of the association of a normal infant with the presence of anti-Rh or other atypical agglutinins in the maternal serum incompatible with the infant's erythrocytes.*

Dockeray and Sachs (1944) in investigating the blood of 61 unselected pregnant women found anti-Rh agglutinins in the sera of 3 of them who later bore apparently normal infants. One infant was group O, Rh positive; the other 2 were not typed and may therefore have been Rh negative. A

single case has also been described by Goldbloom and Lubinski (1946) in which they found Rh antibodies in the maternal blood without the infant showing any symptoms of haemolytic disease.

In this series there were 4 women whose sera contained atypical agglutinins but whose infants were apparently normal.

The notes of these 4 cases and of 3 others which were just prior to the series are given below:

753. F. P., aged 22, 1-gravida, group O, Rh negative, had a normal pregnancy and was delivered at term of a child weighing 6 pounds 14 ounces (group O, Rh positive), which progressed normally. The Rh antibodies in the maternal serum rose to a titre of 16.

1458. M. E., aged 46, 5-gravidae, group A, Rh negative, had had 4 normal deliveries at home. The third baby had died jaundiced on the 11th day. The mother had mitral stenosis but went through pregnancy and labour at term without trouble. The baby (group A, Rh positive) appeared to be completely unaffected. The maternal anti-Rh agglutinins never rose above a titre of 2.

1824. K. K., aged 42, 6-gravidae, group O, Rh negative, had had 5 large infants who had progressed normally. Her pregnancy and delivery at term of a 7-pound baby, group O, Rh positive, were uneventful and the baby was unaffected. The anti-Rh agglutinin titre was 4 and there was also an incomplete Rh antibody present, titre 64 by the Coombs' technique.

2229. D. G., aged 28, 6-gravidae, group A, Rh negative, had had a normal child followed by a premature infant which died on the second day. The third child was normal and the fourth pregnancy resulted in a 2 months' abortion. The fifth pregnancy was uneventful but the 8-pounds baby died of jaundice on the second day. We first saw her at the 34th week of the sixth pregnancy. Rh antibodies (titre 8) were detected but weekly specimens did not show any rise in the titre. A high rupture of the membranes was carried out at the 38th week for hydramnios. The baby weighed 6 pounds 7 ounces, made normal progress, and was found to be Rh negative.

5. F., aged 32, 4-gravidae, group A, Rh positive (R_1r or CDe cde) had 2 normal children followed by an early miscarriage. During the fourth pregnancy she was found to have anti-E (anti-R_2) agglutinins in her serum and labour was induced at the 38th week by rupture of the membranes. The 6 pounds 14 ounces baby was group A, R_1R_2 (CDe cDE), but seemed to be completely normal. The anti-E titre of the maternal serum was 8.

6. H., aged 30, 1-gravida, group O, Rh negative. She had mild hypertension but no albuminuria nor oedema.

The 6 pounds 12 ounces baby (group O, Rh positive) was delivered spontaneously at the 38th week and appeared to be completely unaffected. The titre of the anti-Rh agglutinins in the maternal serum was 2.

7. R., aged 36, 3-gravidae, group O, Rh negative, had 2 stillbirths. She was delivered in the 41st week of her third pregnancy of a live infant weighing 10 pounds 6 ounces (group O, Rh positive). The child was unaffected. The titre of Rh antibodies in the maternal serum was 1 before delivery rising to 8 a week after delivery.

Of the 7 clinically normal infants 1 was in fact Rh negative and therefore was compatible with the maternal serum in spite of the presence of anti-Rh agglutinins. In the other 6, however, the maternal serum was incompatible with the infant's erythrocytes; in 5 cases the antibody was anti-Rh type anti-D, and in the other anti-Rh type anti-E. These infants were clinically normal and without the slightest degree of jaundice or anaemia.

(3) *The possible relation between "physiological" jaundice and blood-group incompatibilities between mother and infant.*

Among the 106 cases of physiological jaundice there were 4 in which the mother's serum contained an atypical antibody incompatible with the infant's erythrocytes. In 2 cases this was an anti-Rh agglutinin, in 1 an Rh antibody of the incomplete type, and in the other the atypical antibody was unidentified.

The notes of these cases are as follows:

1011. A. I., aged 33, 4-gravidae, group A, Rh negative, had had 2 early miscarriages followed by a difficult forceps delivery at term of a baby which died on the fourth day, of traumatic cerebral haemorrhage. The post-mortem examination did not reveal any other abnormality but histological investigation was not carried out. A transfusion was given to the mother for chronic anaemia. The fourth pregnancy was normal and there was delivery at term of an 8 pounds 12 ounces baby (group O, Rh positive). The child developed slight jaundice on the 2nd day but this was less on the third day and soon faded completely. The haemoglobin was 122 per cent and the blood film did not show any abnormality. Weak Rh antibodies, titre 2, were present in the maternal serum.

1379. I. P., aged 17, 1-gravida, group A, Rh positive, had a normal pregnancy and a 7 pounds 7 ounces baby (group O, Rh positive), born at term, developed only mild physiological jaundice on the fourth day. A strong atypical antibody, titre 16, was present in the maternal serum. It was more active at 37°C. than in the cold, and did not seem to be connected in any way with the Rh system, nor with the sub-groups of A, with M and N, or with P. Unfortunately the woman was very uncooperative and we were unable to obtain serum to carry out further tests.

2270. M. W., aged 23, 1-gravida, group AB, Rh negative, had a normal pregnancy and labour at term. The 7 pounds 13 ounces baby (group B, Rh positive), developed transient jaundice on the 4th day. The haemoglobin was 124 per cent and progress was satisfactory. The mother's serum contained no anti-Rh agglutinin, only a weak incomplete Rh antibody, titre 2. The infant's red cells gave a negative Coombs test.

2450. M. A., aged 24, 2-gravidae, group A Rh negative, had had a normal first baby. She was induced at the 39th week of the second pregnancy for a rising titre of Rh antibodies. The baby weighed 6 pounds 5 ounces (group A, Rh positive), became slightly jaundiced on the fourth day, but this was fading and the haemoglobin was 100 per cent on the sixth day. The maternal Rh antibody-titre rose to 32 after delivery.

It is possible that in the above 4 cases the jaundice was due to the maternal antibody and that they should more properly be regarded as mild cases of haemolytic disease of the newborn. On the other hand they were clinically indistinguishable from physiological jaundice and there is no reason why this syndrome should not occur in cases where there is an atypical antibody quite independently of the presence of such an antibody.

In 25 instances where the infant was suffering from physiological jaundice the maternal serum contained anti-A or anti-B agglutinins incompatible with the infant's erythrocytes (heterospecific pregnancy). There were 359 cases of heterospecific pregnancy in the series, so that the percentage showing physiological jaundice in this group is not significantly higher than the 5.25 per cent found for the whole series. However, if the 18 cases in which the jaundice became apparent by the second day after delivery are considered, in 11 there were anti-A and anti-B agglutinins in the maternal serum incompatible with the foetal erythrocytes. Thus this confirms the view of Halbrecht that such incompatibilities play some part in the aetiology of the type of neonatal jaundice named by him icterus praecox.

In the remaining 77 cases of physiological jaundice no serological incompatibilities between mother and infant were detected.

(4) *The possibility of a serological reason for some of the miscarriages and stillbirths usually relegated to the category "cause unknown".*

There were only 20 stillbirths and 14 miscarriages in the series*

Anti-Rh agglutinins were present in the sera of 4 of the mothers having stillborn

* Excluding the 2 stillbirths diagnosed as due to haemolytic disease of the foetus and reported above.

children. In 3 the infant was not typed, but was probably Rh positive as the maternal antibodies increased in titre. In the other the infant was Rh negative. Details of these 4 cases are given below:

68. E. W., aged 29, 3-gravidae, group O, Rh negative, had post-partum haemorrhage necessitating transfusion after the second delivery. She developed pre-eclamptic toxaemia at the 30th week of the third pregnancy, the baby dying *in utero* 3 weeks later.

Medical induction of labour resulted in delivery of a 2 pounds 11 ounces macerated foetus at the 35th week. Anti-Rh agglutinins, rising from 0 to a titre of 4 were present in the maternal serum; the foetus was not grouped or Rh-typed.

109. M. C., aged 32, 4-gravidae, group A, Rh negative, had had a normal child followed by an early abortion and then by a stillbirth, cause unknown. The present pregnancy was normal but she was delivered of a macerated foetus at term. The placenta did not show evidence of erythroblastosis. (Notes kindly supplied by Mr. Bruce Dewar.) The foetus was not grouped or Rh-typed. However the foetus was, no doubt, Rh positive as the titre of Rh antibodies in the maternal serum rose from 0 in early pregnancy to 8 after delivery.

1158. M. H., aged 38, 5-gravidae, group O, Rh negative, had had 3 normal children followed by a full-time child delivered at home who died of jaundice on the second day. The 5th pregnancy resulted in a macerated foetus delivered at home at 37 weeks. We had not seen her at the hospital clinic for several weeks and have no details of the maturity when foetal death occurred. A few days after delivery the titre of maternal Rh antibodies was 32.*

2922. H. K., aged 38, 13-gravidae, group A, Rh negative, had 11 living children. The third pregnancy resulted in 1 living and 1 stillborn premature twin and the child of the 4th pregnancy was stillborn (cause unknown). The 13th pregnancy was complicated by mild hypertension and oedema but albuminuria did not develop. Labour was induced at the 39th week by rupture of the membrane on account of the presence of Rh antibodies but labour did not start until 3 days later following concealed and revealed accidental haemorrhage necessitating transfusion. The 8-pounds baby was stillborn but the foetal heart sounds had been satisfactory until bleeding started. This child was found to be group A, Rh negative, and so the stillbirth was not connected with the presence of anti-Rh agglutinins (titre 2) in the maternal serum.

Of these 4 stillbirths, therefore, 3 may have been due to haemolytic disease of the foetus although in the 1 there was the added complication of toxaemia of pregnancy of the mother. The fourth was apparently due to the accidental haemorrhage. Of the remaining 16, 5 were due to congenital defects, 1 to extreme prematurity, 2 to prolapsed cord, 1 to accidental haemorrhage, 1 to syphilis, 1 to cerebral haemorrhage and marked generalized oedema (this infant was twin to one which died during the neonatal period from cerebral haemorrhage) and in 5 the cause was unknown. It was not possible to type the foetus in every case but in the majority which were typed there was no incompatibility between the maternal serum and the infant's erythrocytes on the ABO system.

There did not seem to be a serological cause for any of the 14 miscarriages for there was no Rh or ABO incompatibility detected between mother and foetus where it was possible to type the foetus, and in no case was there an anti-Rh or other atypical agglutinin, nor an exceptionally potent anti-A or anti-B agglutinin present in the maternal serum in those cases in which it was not possible to type the foetus. These findings would seem to disagree with Levine's hypothesis that miscarriages are often due to heterospecific pregnancy. This is not necessarily so, however, for the number of heterospecific pregnancies (359) in the series is less than the expected number, and as bookings were seldom made

* The following year labour was induced at the 37th week for rising Rh antibodies. The 6 pounds 14 ounces baby developed icterus gravis but survided after transfusion. This 6th pregnancy is not included in the series.

before the 12th week of pregnancy early miscarriages may account for the missing heterospecific pregnancies. (For a full discussion of this point, see Boorman and Dodd, *Annals of Eugenics*, to be published.)

(5) *The relation between parity and the above clinical conditions of the infant.*

Haemolytic disease of the foetus. In the case of haemolytic disease where the mother was Rh positive and the agglutinin anti-c, the affected child was the second in the family. However, the mother had been transfused following the birth of her first infant and these transfusions had probably helped to sensitize her.

Of the 336 Rh negative women, 186 were primigravidae and there was no clinical case of haemolytic disease of the foetus among their infants. Moreover, none of the first children of all 336 Rh negative women was apparently affected although there were 11 families in which subsequent children were affected with the disease. As would be expected, there was no case of haemolytic disease of the foetus where the infant was Rh negative and therefore unable to stimulate or react with Rh antibodies. Thus it is the group of 211 negative women with Rh positive infants which has to be considered. This total includes 11 where the infant was not typed and so may have been Rh positive. In 1 case a second child was affected but here the mother had had 2 transfusions (of blood which had not been Rh typed, but was probably Rh positive), after delivery of the first infant. The incidence of haemolytic disease of the foetus was high after the third pregnancy as is seen from Table III. Some idea can be obtained from this table also, with regard to the probability of Rh negative women with Rh positive husbands having infants affected with haemolytic disease of the foetus, for where the third or subsequent child was Rh positive it was affected with the disease in 28.9 per cent of cases. These families include some where the husband is heterozyogous as well as all those where he is homozygous Rh positive. All children of the homozygous husband must be Rh positive, while there is a chance of 50 per cent of the children of heterozygous husbands being Rh negative. In families where the mother is Rh negative and the husband homozygous Rh positive it is likely that the third child or subsequent children will be affected with haemolytic disease; where the husband is

TABLE III.

Clinical Condition of the Infant in Cases Where the Mother was Rh Negative and the Infant Rh Positive (or in a few Cases not Typed).

Place in family		Clinical condition of Infant					
		Normal	Stillbirth	Miscarriage	Physiological jaundice	Haemolytic disease	Total
1	Number	104		3	8		115
	Per cent	90.4		2.6	7.0		54.5
2	Number	47		1	4	1	53
	Per cent	88.6		1.9	7.6	1.9	25.1
3	Number	9	1			4	14
	Per cent	64.3	7.1			28.6	6.6
4	Number	19	2		1	7	29
or over	Per cent	65.5	6.9		3.5	24.1	13.8
Total	Number	179	3	4	13	12	211
	Per cent	84.8	1.4	1.9	6.2	5.7	100.0

heterozygous Rh positive, however, it may be much later in the family before a child affected with haemolytic disease is born.

Physiological Jaundice.

There was no connexion between parity and the likelihood of the infant to be affected with physiological jaundice (see *Annals of Eugenics,* to be published).

Miscarriages and Stillbirth.

The miscarriage and stillbirth-rate did not alter significantly with parity except that the miscarriage-rate was higher after the sixth pregnancy. This was because the total numbers in the groups 6-para or over were very small, as the fact that in the series there were 2 or 3 women who habitually aborted for various reasons was enough to increase significantly the miscarriage-rate (see *Annals of Eugenics,* to be published).

CONDITION OF THE MOTHER.

(1) *The proportion of Rh negative women with Rh positive infants who form Rh antibodies.*

Of the 336 Rh negative women included in the series, 211 had Rh positive infants. One hundred and fifteen of these were primigravidae, only 1 of whom developed Rh antibodies and then not until the tenth day of the puerperium (the baby in this case was normal). Nineteen of the remaining 96 developed antibodies and 11 of the infants were affected with haemolytic disease of the foetus.

(2) *The time at which Rh agglutinins are first detected in the maternal serum during pregnancy.*

Four of the 24 atypical antibodies found among the 2,000 cases tested were present in the maternal serum early in pregnancy. One of these, titre 2, through pregnancy and puerperium, was in a woman whose infant proved to be Rh negative and it was no doubt a legacy from her eleventh pregnancy, 4 years previously, when the infant was Rh positive. Two of the others showed a rise in the titre during pregnancy, the titre after delivery rose to 1,000 in each case. In the fourth case the antibody remained at 2 until the 26th week when a macerated foetus was spontaneously delivered, subsequently the titre rose to 128.

Ten Rh negative women who had had no Rh antibodies early in pregnancy were found to have developed them by the 34th week. There was a fairly wide range of titre, from 1 to 64, but 5 out of the 10 had titres of only 1 or 2. In a further 8 antibodies were not detected until delivery and in the 2 remaining not until the 10th day of the puerperium; 1 of the latter was incomplete anti-Rh titre 2 and the other the unidentified antibody, titre 16 (case 1378).

Rh agglutinins are rarely found in the maternal serum early in pregnancy and when present they are often a legacy from the previous pregnancy and so do not indicate whether or not the present foetus is Rh positive. However, should the titre rise during the pregnancy this means that the foetus is likely to be Rh positive and will most probably be affected with haemolytic disease. When antibodies first appeared in the serum late in pregnancy, especially during the last week or so, the infant although Rh positive, is not invariably clinically affected. However, a high titre of atypical antibodies at any period during the pregnancy usually means that the infant will be affected although sometimes only mildly. Now that various tests for the "incomplete" antibody have been devised, both the agglutinin titre and the incomplete antibody titre should be recorded, as both types of antibody may affect the foetus.

In our series we had only 2 cases where the antibody did not appear in the maternal

serum until the tenth day of the puerperium; in both cases the woman was a primigravida and the infant was not affected.

(3) *The possible association of pre-eclamptic toxaemia and eclampsia of pregnancy with a blood group incompatibility between mother and foetus.*

There were 93 women who had had toxaemia of pregnancy, including 2 cases of mild eclampsia. The distribution of the ABO groups among these 93 women seems to be quite normal and therefore there is no reason for concluding that there was any connexion between ABO incompatibilities and toxaemia of pregnancy. Sixteen of the women were Rh negative, a percentage of 17.2 which is slightly higher than for the whole series but not significantly so. Moreover, in only 1 case was there an anti-Rh agglutinin in the maternal serum incompatible with the foetal erythrocytes. There was a connexion between party and toxaemia, our findings quite definitely confirming the known fact that toxaemia of pregnancy is most usually associated with a first pregnancy. Sixty-one of the 93 cases were primigravidae and if those who had only had an abortion previously are also considered as primigravidae there were 70 out of 93. It may be of interest that in this series the number of primigravidae (including those having a previous abortion) who had toxaemia of pregnancy was 70 out of 1,223 (5.7 per cent). This is very close to the percentage (5.4 per cent) found in the especially fed group of the People's League of Health experiment, and lower than that found by them in an untreated group (7.4 per cent). Ninety of the 93 women having toxaemia of pregnancy had normal infants; of the 3 remaining, 2 had "stillbirths" and 1 an infant affected with physiological jaundice. One of the "stillbirths" had a congenital heart lesion, and the other was Case No. 68, reported above, where there was added complication of Rh antibodies in the maternal serum. Thus, in this series, toxaemia of pregnancy seemed to have little or no adverse effect on the baby. This may be due to the fact that we were fortunate enough to be able to admit to hospital all women showing early manifestations of the disease.

Additional Observations.

The Condition of the Baby.

(6) *Neonatal Death.*

There were 26 neonatal deaths in the series. Five are reported above as due to haemolytic disease of the foetus with kernicterus; there were 6 caused by congenital defects (see below); 5 by prematurity associated with atelectasis; 4 were due to cerebral haemorrhage; 5 to infection, and 1 was jaundiced from the second day, the postmortem findings showing extensive brain damage, some liver damage and general congestion, but no evidence of erythroblastosis.

Apart from the 5 due to haemolytic disease there was no proved connexion between the serology of these cases and the neonatal death of the infant.

(7) *Congenital Defects.*

There were 15 children in the series with congenital defects. Five were stillborn (4 anencephalic and 1 congenital heart lesion). Six died in the neonatal period (2 congenital heart lesions, 2 hydrocephalics, 1 diaphragmatic hernia and 1 oesophageal atresia). The remaining 4 survived (1 meningomyelocoele, 1 hare-lip, 1 cleft-palate and 1 meningocoele).

It seems unlikely that these defects had a serological cause as in no case was an Rh antibody detected in the maternal serum, and in only 3 cases was there an incompatibility between the mother's serum and

the infant's erythrocytes on the ABO system. However, a large series of congenital abnormalities would have to be investigated before it could be proved how great a proportion of these was connected with serological incompatibilities between the mother and the infant.

(8) *Sex.*

It has been suggested by Halperin, Jacobi and Dubin (1945) that the prognosis for an infant suffering from haemolytic disease is worse if the infant is male. Of the 8 children affected with the disease, reported above, who recovered 5 were male. Here again a larger series would be necessary before any dogmatic statement could be made.

The Condition of the Mother.

(4) *Accidental Haemorrhage.*

Burch (1945) found that among 10 cases of accidental haemorrhage 5 of the women were Rh negative, 3 having anti-Rh agglutinins in their serum. She concluded that while the subject needs further investigation it seemed possible that women with Rh antibodies were exceptionally prone to accidental haemorrhage.

There were only 5 cases in our series showing accidental haemorrhage. Bleeding after the 28th week in the absence of placenta praevia has been classified as accidental haemorrhage. The small number of cases in the series is due to the fact that cases of minor bleeding were, in accordance with the current practice, not designated accidental haemorrhage, but were relegated to the category "cause unknown" without vaginal examination being made for diagnosis of placenta praevia. In 4 of the cases there was no blood group incompatibility between the mother and the infant, although in 1 of them anti-Rh agglutinins were present in the maternal serum, presumably as the result of iso-immunisation of the mother during a previous pregnancy, as the present infant was Rh negative. In the other case the mother was group B and the baby group A. However, this is far too small a number on which to base any conclusions.

(5) *Previous Stillbirths and Miscarriages.*

Of the 284 families in which there were previous stillbirths or miscarriages there were 119 where the mother was group O, 121 where the mother was group A, 34 where she was group B and 10 where she was group AB. This is not significantly different from the expected blood group distribution. On the other hand there were 56 Rh negative mothers, a percentage of 19.7 per cent, which is higher than for the whole series. This is even more marked when only those families who had more than 1 previous miscarriage or stillbirth are considered, the percentage of Rh negative mothers is then 23.5 approximately. Table IV gives details of the Rh negative families where there was more than 1 previous stillbirth or miscarriage. It will be seen that in 6 there were anti-Rh agglutinins present in the maternal serum, and in 4 the present child was diagnosed as suffering from haemolytic disease of the foetus.

Discussion.

Perhaps the most interesting finding arising from the investigation, and one which can only be discovered from the testing of a large unselected series, is the fact that anti-Rh agglutinins can occur in the maternal serum associated with a normal Rh positive infant. In our series we found 11 such cases (4 of these infants showed a mild transient physiological jaundice). It is possible that in the future a thorough study of similar cases may yield valuable information which may suggest a new approach

to the treatment for haemolytic disease of the foetus.

In view of the possibility of finding a solution to the problem of haemolytic disease we feel that the practice of some form of birth control would be preferable to the sterilization of an Rh negative woman with a history of this disease among her children, especially if she is young. It should also be borne in mind that circumstances might arise in which she might have normal infants by another husband who was Rh negative or Rh positive of the heterozygous type.

Ideally the husbands of all Rh negative women after the first pregnancy should be tested in order to find out whether they are Rh positive and if so whether homozygous or heterozygous. At the moment, however, this is not practicable owing to a shortage of the appropriate sera. Such sera are only very rarely produced and then not always in high enough titre to be suitable for typing sera. Moreover, as with all Rh agglutinating sera, the serologist is absolutely dependent for his supply upon the co-operation of the clinician in persuading the patient to give her blood for this purpose. Until supplies of the rare sera are more plentiful, therefore, it is probably best to reserve them for the genotyping of husbands in families where a case of haemolytic disease of the foetus has already occurred and the parents are anxious to have another child if possible.

All Rh negative women who have had more than 1 pregnancy should have their sera tested for Rh antibodies at intervals during pregnancy, especially between the 34th week and term, as it is during this period that these antibodies are most likely to be detectable. Should such an antibody be found the question arises whether or not it is advisable to induce labour. This is ultimately, of course, the responsibility of the clinician but the serological findings can

TABLE IV.

Details of the Obstetric History of the 17 Rh Negative Women who had more than one Previous Stillbirth or Miscarriage.

No.	Mother's group	Baby's group	Immune antibody	Pregnancies 1	2	3	4	5	6	7	8	9	10	11	12	13
201	O neg.	O pos.	Rh	N.	S.B.	S.B.	H.D.									
260	A′	A neg.		N.	Mis.	S.B.	N.	Mis.	N.							
438	A neg.	O neg.		Mis.	Mis.	N.										
676	O neg.	O neg.		N.	Mis.	N.	N.	N.	Mis.	N.	N.	N.	N.	N.		
732	A neg.	O pos.		Mis.	N.	Mis.	N.									
943	O neg.	O pos.		Mis.	Mis.	Mis.	Mis.	N.								
430	O neg.	B pos.	Anti-B	S.B.	N.	Mis.	N.									
259	O′	O pos.		Mis.	N.	Mis.	N.									
451	A′	A pos.		N.	S.B.	N.	S.B.	N.								
811	B neg.			Mis.	Mis.	S.B.										
625	AB neg.	A pos.	Rh	Mis.	S.B.	N.	N.	N.	H.D.	H.D.						
181	A neg.	O pos.	Rh	N.	Mis.	Mis.	H.D.									
922	A neg.	A neg.	Rh	N.	N.	N. Mis.	S.B.	N.	N.	N.	N.	N.	N.	N.	N.	S.B.
582	O neg.	B pos.	Anti-B	N.	S.B.	Mis.	Mis.	N.								
584	O neg.	A pos.	Anti-A.	Mis.	Mis.	Mis.	N.									
109	A neg.		Rh	N.	Mis.	S.B.	S.B.									
1011	A neg.	O pos.	Rh	Mis.	Mis.	N.	J.									

N. = Normal Mis. = Miscarriage S.B. = Stillbirth
H.D. = Haemolytic Disease J. = Jaundiced

give him some help in making the decision. If an antibody is detectable early in pregnancy and does not rise in titre, it is possible that the present foetus is Rh negative and it is a legacy from a previous pregnancy, and therefore there is no reason for induction. Occasionally, however, the antibody titre does not rise even when the foetus is Rh positive. The testing of the father may be helpful for, should he prove to be homozygous Rh positive, the foetus must be Rh positive and liable to be affected with haemolytic disease and so it might be wise to induce early. A rising titre of antibodies from early pregnancy to the 26th or 28th week almost always means that the foetus will be affected with the disease. In this case, induction can be undertaken as soon as the foetus has attained a weight and maturity compatible with life. Should antibodies not appear until very late in pregnancy it is probably best to allow the pregnancy to go to term as there is a possibility that the infant, although Rh positive, may be unaffected (there were 2 cases where the infant was normal and 2 where it showed only mild jaundice in our series) and it is not worth exposing it to the dangers of prematurity unnecessarily.

We have not confirmed Javert's finding that signs of distress in labour are common in the affected babies, and feel that, in the absence of any other indication, Caesarean section should not be undertaken. It does not seem justifiable to subject the mother to this extra risk for the sake of a baby which has a considerable chance of developing kernicterus, even if delivered prematurely and transfused.

Summary.

A serological and clinical survey of 2,000 mothers and their 2,024 infants was made.

The mothers were tested serologically during pregnancy as well as at delivery.

The association of normal infants with a maternal serum containing Rh antibodies incompatible with the foetal erythrocytes was found to be more common than has hitherto been believed.

The possible connexion between various clinical conditions and serological incompatibilities is discussed.

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We are indebted to the Registrar-General for allowing us access to his unpublished figures for 1944.

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Studies in Prematurity, Stillbirth and Neonatal Death

Part I. Factors Affecting Birth-weight and Outcome

BY

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Introduction.

In the following studies an attempt is made to evaluate the principal aetiological factors influencing the incidence of prematurity, infant deaths and stillbirths. It is based on the records of 7,599 births in in Simpson Memorial Pavilion, Royal Infirmary, Edinburgh, during the 3 years 1943 to 1945 inclusive.

During the past 15 years a large number of similar studies have been made, particularly in America, with widely divergent conclusions. In a detailed review of the literature on prematurity by Anderson and Lyon (1939), the percentage of premature births attributed by different authors to toxaemia of pregnancy is seen to range from 1.4 per cent (Capper 1928) to 29.9 per cent (Dunham and McAlenney, 1936). The figure for antepartum haemorrhage was found to be 1.5 per cent by Brown (1917) and 18.2 by Cook (1921). Heart disease in the mother was found in 8.3 per cent of cases by Rapisardi (1931) but in only 0.1 per cent by Israel and Kemkes (1927) while premature births attributed to unexplained causes were placed as low as 18.8 per cent by Rapisardi and as high as 76.9 per cent by Israel and Kemkes. The main reason for these gross discrepancies would seem to be as follows:

1. The absence of adequate controls. In many of the studies made on prematurity and infant deaths, no control group of mature healthy infants has been included for comparison. Any abnormality or disease occurring during the mother's pregnancy or delivery is apt to be called the cause of the prematurity or death of the infant, though an equal incidence of such abnormalities might well have been found in a control group if this had been included for comparison.

2. Failure to differentiate between emergency and booked cases. The maternity practice of a hospital can be divided into two main groups:—

(*a*) "Booked" cases who have made arrangements in advance for confinement in the hospital. In this country in recent years this group has included a high proportion of primiparae, with a small number of multiparae who are admitted because of previous bad obstetrical history or chronic disease, or for social reasons. These mothers have usually received antenatal care.

(*b*) "Emergency" cases, who are admitted in or shortly before the commencement of labour, because of some complication or other urgent reason.

In any attempt to use hospital patients as a sample from which general conclusions can be drawn applicable to the population as a whole, only booked primiparae should be included.

3. The omission in many studies of all consideration of stillbirths. As McNeil (1942) has stated:—

"It is necessary to place alongside any figures of neonatal mortality the corresponding stillbirths. This is especially important in any international comparison of infant mortality rates. Unless this is done, serious errors in the calculation of infant deaths will be made. Further, the dividing line between stillbirths and neonatal deaths, usually so sharply drawn, is misleading, because the same lethal processes that destroy infant life during birth continue to operate with great power after birth, and indeed are responsible for the majority of neonatal deaths."

4. The adoption by different authors of varying criteria of prematurity and of viability. For instance, in a survey carried out by Tyson (1934) on 4,663 deliveries, the premature infant is taken to be one of between $4\frac{1}{2}$ months gestation and 38 weeks, as estimated presumably from the mother's statements and clinical examination. He excluded from his premature group a number of babies who by the usual criterion of weight would have been included, because they were estimated to be full time. Another American author, writing in the same year (Clifford, 1934); in an analysis of the influence of obstetric factors on the viability of 958 premature infants, defines a "premature" baby as one weighing less than 5 pounds, and places those between 5 pounds and 6 pounds in an "immature" group. At the present time, the definition laid down by the International Medical Committee of the League of Nations on a weight basis has gained general acceptance. This defines a premature infant as being one with a birth-weight of $5\frac{1}{2}$ pounds (2,500 g.) or under. Attempts have been made to define a lower as well as an upper limit for the birth-weight of a premature baby. In certain surveys infants below 1,500 g. (3 pounds 4.8 ounces) have been considered "non-viable" and excluded from the sample. Peckham (1938) in a series of statistical studies on prematurity from the Johns Hopkins Hospital, omits as "previable" all infants less than 1,500 g. in weight, or 35 cm. in length. Recently the suggestion has been put forward by Henderson (1945) that $2\frac{3}{4}$ pounds (1,250 g.) be taken as the lower limit of viability. Now Dunham and McAlenny (1936), in a study of 5,000 births, found that 35 per cent of babies between 1,000 and 1,499 g. at birth survived their stay in hospital, and 1.2 per cent of those below 1,000 g. To call an infant born alive "previable" appears to be a contradiction in terms, and there seems to be little justification for setting a lower limit to the definition of prematurity when applied to liveborn infants. Where stillbirths are concerned, it is more difficult to draw the line between a premature stillbirth and an abortion. Here both weight and estimated gestation must be taken into account.

Procedure.

During the 3 years 1943 to 1945, nearly 8,000 births occurred in the Simpson Maternity Pavilion, Edinburgh. A special code card was designed, on to which was entered details from the obstetric and infant records of every stillbirth, infant death and premature birth occurring during the period. A random 1-in-10 sample was also taken of mature infants born in the hospital and surviving their discharge, to serve as a control group. In making up totals and calculating rates, the figures for mature surviving infants have where necessary been multiplied by 10 to restore the original proportions. Due allowance has been made for this in the tests of significance used.

The following data were obtained for each case:—

1. General information about the mother, such as age, parity, whether married or single, a history of previous pregnancies, and whether booked or emergency.

2. Social data, including occupation of husband, average weekly income and employment of mother during pregnancy.

3. Information regarding the pregnancy and delivery in question; any complicating illnesses or accidents, length of labour and mode and complications of delivery.

4. Information concerning the baby while in hospital; weight at birth and estimated time of gestation, method of feeding in hospital, any pathological conditions occurring in hospital diagnosed clinically in those who survived.

5. Follow-up of the baby as far as possible from records of the welfare clinic which serves all babies born in this hospital. Data recorded included details of feeding, weight and progress.

6. In all stillbirths and deaths, clinical diagnosis and pathological findings at autopsy.

7. Detailed information regarding income, housing, efficiency of the mother was obtained in a smaller sample by home visiting.

The data recorded on the individual code cards were sorted and analyzed.

Outcome according to birth-weight is considered in this paper, and also the various factors affecting the weight of the infant. The next paper in this series deals with delivery and its hazards, and the third with a detailed analysis of deaths and stillbirths.

Further papers will consider the effect of social factors on prematurity, and infant wastage, and the progress of babies in hospital and after discharge.

Birth-weight and Outcome.

In this paper an infant is regarded as premature if its birth-weight is not more than 5½ pounds. Table I shows the proportion of premature and of mature infants born to primiparae. During the 3-year period under review, the prematurity-rate amongst all primiparae was 8.6 per cent, including 1.7 per cent of babies weighing 3½ pounds or less. At the other end of the scale, there was 0.3 per cent of infants over 10 pounds in weight, regarded as "post-mature." The remaining 91.1 per cent fell within the weight limits of maturity. These figures refer to a hospital sample, which contains booked and emergency cases, as well as multiple and illegitimate births, in proportions different from their incidence in the general population of first births. The last two columns give the figures for booked married women. The prematurity-rate there shown, 5.9 per cent, most nearly represents that to be expected in the population as a whole for legitimate first pregnancies.

Prematurity-rates: Multiparae.

Since multiparae are not normally admitted to hospital unless there is some special reason, such as complication of pregnancy or delivery, bad obstetrical history, or social difficulties, it is not possible to obtain from hospital cases a rate in any way representative of that in the general population.

Outcome According to Birth-weight: Primiparae.

Table II gives the "outcome"—whether the baby survived, died or was stillborn—for all primiparae in each half-pound weight group. These data are plotted in Fig. 1. The survival rate is seen to rise rapidly with increasing weight up to the 5 pounds 9 ounces to 6 pounds group. It then remains steady at about 97 per cent until

TABLE I.

Distribution of Birth-weights Among First-born Infants.

Birth-weight				All primiparae		Unmarried mothers		Multiple births		Booked legit. single births	
Pounds	Ounces	Pounds	Ounces	Per cent	Cumulative	Per cent	Cumulative	Per cent	Cumulative	Per cent	Cumulative
Less than	3	9		1.7	1.7	1.2	1.2	9.8	9.8	1.1	1.1
3	9 to	5	8	6.9	8.6	6.9	8.1	49.9	60.7	4.8	5.9
5	9 to	10	0	91.1	99.7	91.7	99.8	40.3	100.0	93.8	99.7
More than		10	0	0.3	100.0	0.2	100.0			0.3	100.0

TABLE II.

All Primiparae: Outcome According to Birth-weight

Birth-weight				Number of cases	Per cent lived	Per cent died	Per cent stillborn	Per cent stillborn of total wastage
Pounds	Ounces	Pounds	Ounces					
1	1 to	1	8	3	—	—	100.0	
1	9 to	2	0	12	—	50.0	50.0	52.9
2	1 to	2	8	19	—	52.6	47.4	
2	9 to	3	0	21	19.0	42.9	38.1	51.4
3	1 to	3	8	32	43.8	25.0	31.0	
3	9 to	4	0	40	47.5	22.5	30.0	55.3
4	1 to	4	8	69	75.3	11.6	13.1	
4	9 to	5	0	91	80.2	7.7	12.1	59.0
5	1 to	5	8	143	85.3	6.3	8.4	
5	9 to	6	0	332	93.4	3.3	3.3	61.9
6	1 to	6	8	600	96.7	0.8	2.5	
6	9 to	7	0	878	96.8	0.8	2.4	73.9
7	1 to	7	8	838	97.8	0.6	1.6	
7	9 to	8	0	852	98.6	0.4	1.0	79.4
8	1 to	8	8	472	95.4	0.8	3.8	
8	9 to	9	0	357	98.0	0.6	1.4	
9	1 to	9	8	177	96.1	1.1	2.8	73.3
9	9 to	10	0	31	96.8	—	3.2	
10	1 to	12	0	15	66.7	—	33.3	100.0
Total				—	94.2	2.1	3.7	63.7
Total number of cases				4982	4693	105	184	

the "post-mature" group of over 10 pounds is reached. Fig. 2 gives the same information in a different way. Here the percentage of all survivors occurring below the stated weight levels is plotted. Similar curves are plotted for "died" and "stillborn." The figure shows that, on the whole, the babies who died tend to be smaller than those stillborn, and these again are smaller than those who survived. Among the survivors, 6 per cent were premature. The corresponding figures for the stillbirths and the deaths are 44 per cent and 62.9 per cent respectively.

In the smaller weight groups, stillbirths form about 50 per cent of the total wastage. The proportion of stillbirths rises with birth-weight, reaching 80 per cent in the mature group and 100 per cent in post-mature infants. The data for both primi-

parae and multiparae are set out in Fig. 3. The line for the latter is similar to that of the primiparae, but on rather a higher level. This is probably due, entirely or in part, to the older age-composition of the multiparous mothers, since, as shown in a later section, the proportion of stillbirths tends to rise with maternal age.

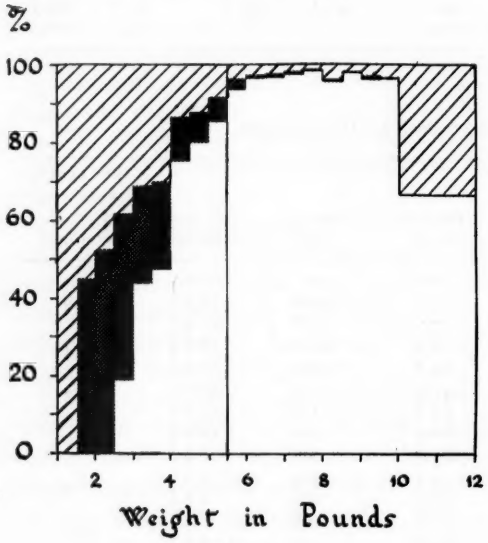

FIG. 1.
Outcome by birth-weight
Shaded—Stillbirths.
Black—Deaths.
White—Lived.

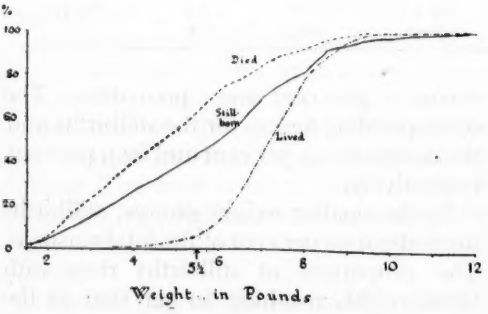

FIG. 2.
Cumulative percentage birth-weight curves.

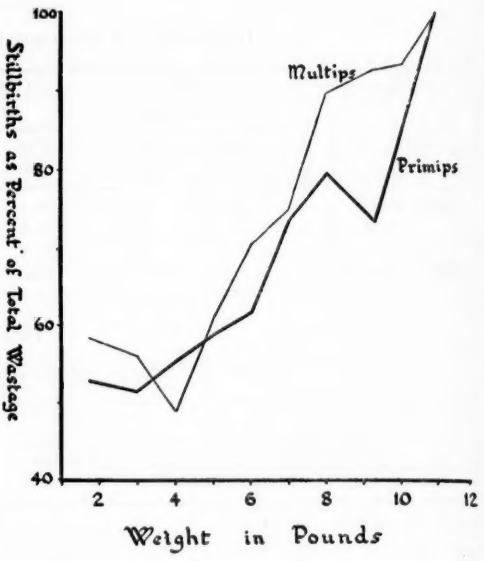

FIG. 3.
Stillbirths as percentage of total wastage.

Outcome According to Birth-weight: Multiparae.

Table III gives the outcome, by weight, for multiparae. This shows a similar picture to that for first births, except that the survival rates at any given birth-weight level tend to be lower. This is what would be expected because of the higher proportion of emergency and complicated cases among the multiparae admitted to hospital.

FACTORS AFFECTING BIRTH-WEIGHT.

1. COMPLICATIONS OF PREGNANCY.

The complications of pregnancy recorded in this investigation fall under three main headings:—

(*a*) Complications of the pregnancy itself, *e.g.*, toxaemias, pyelitis of pregnancy, hydramnios.

(*b*) Chronic maternal diseases coincident with the pregnancy, *e.g.*, cardiac disease, syphilis, diabetes.

TABLE III.

All Multiparae: Outcome According to Birth-weight

Birth-weight				Number of cases	Per cent lived	Per cent died	Per cent stillborn	Per cent stillborn of total wastage
Pounds	Ounces	Pounds	Ounces					
1	1	to 1	8	5	—	40.0	60.0	58.5
1	9	to 2	0	12	—	33.3	66.7	
2	1	to 2	8	24	—	45.8	54.2	56.0
2	9	to 3	0	25	8.0	44.0	48.0	
3	1	to 3	8	35	22.9	31.4	45.7	49.0
3	9	to 4	0	58	50.0	29.3	20.7	
4	1	to 4	8	59	66.1	13.6	20.3	61.3
4	9	to 5	0	54	72.2	9.3	18.5	
5	1	to 5	8	88	81.8	8.0	10.2	70.7
5	9	to 6	0	128	85.9	3.9	10.2	
6	1	to 6	8	353	93.4	2.0	4.6	75.0
6	9	to 7	0	305	95.1	1.3	3.6	
7	1	to 7	8	511	95.9	1.0	3.1	89.5
7	9	to 8	0	359	97.5	0.3	2.2	
8	1	to 8	8	240	95.8	0.4	3.8	94.4
8	9	to 9	0	169	94.7	0.6	4.7	
9	1	to 9	8	96	93.7	—	6.3	100.0
9	9	to 10	0	73	95.9	—	4.1	
10	1	to 12	0	23	87.0	—	13.0	
Total				—	89.0	3.8	7.2	65.3
Total number of cases				2617	2329	100	188	

TABLE IV.

All Primiparae: Complications of Pregnancy by Birth-weight

Birth-weight				Number of cases	With complications	Without complications	Per cent with complications
Pounds	Ounces	Pounds	Ounces				
1	1 to	2	8	34	20	14	58.8
2	9 to	3	8	53	33	20	62.3
3	9 to	4	8	109	69	40	63.3
4	9 to	5	8	234	104	130	44.4
5	9 to	6	8	932	344	588	36.9
6	9 to	7	8	1716	358	1358	20.9
7	9 to	8	8	1334	252	1082	18.9
8	9 to	10	0	555	124	431	22.3
10	1 to	12	0	15	2	13	13.3
Total				4982	1306	3676	26.2

(*c*) Acute illness or injury occurring within 3 months of delivery. "Total complications" comprise all cases falling into any of the above groups.

Total Complications.

Tables IV and V give the total complication-rate in each weight-group for primiparae and for multiparae. These rates are

TABLE V.

All Multiparae: Complications of Pregnancy by Birth-weight

Birth-weight					Number of cases	With complications	Without complications	Per cent with complications
Pounds	Ounces		Pounds	Ounces				
1	1	to	2	8	41	27	14	65.9
2	9	to	3	8	60	46	14	76.7
3	9	to	4	8	117	83	34	70.9
4	9	to	5	8	142	80	62	56.3
5	9	to	6	8	481	207	274	43.0
6	9	to	7	8	816	316	500	38.7
7	9	to	8	8	599	204	395	34.1
8	9	to	10	0	338	115	223	34.0
10	1	to	12	0	23	2	21	8.7
Total					2617	1080	1537	41.3

shown graphically in Fig. 4. The complication-rate falls strikingly with increase in birth-weight. In other words, a mother with a complication of pregnancy is more likely to give birth to a small baby than a woman without complications. Tables VI and VII deal with the same facts in rather a different way. They show, for primiparae and multiparae respectively, the cumulative percentage weight-composition of babies whose mothers had complications, as compared with the no-complication group. It will be seen from Table VI that the prematurity rate for the group with complications (17.3 per cent) is over 3 times that of the group without complications (5.6 per cent), and the percentage of infants of $6\frac{1}{2}$ pounds or under is twice as great

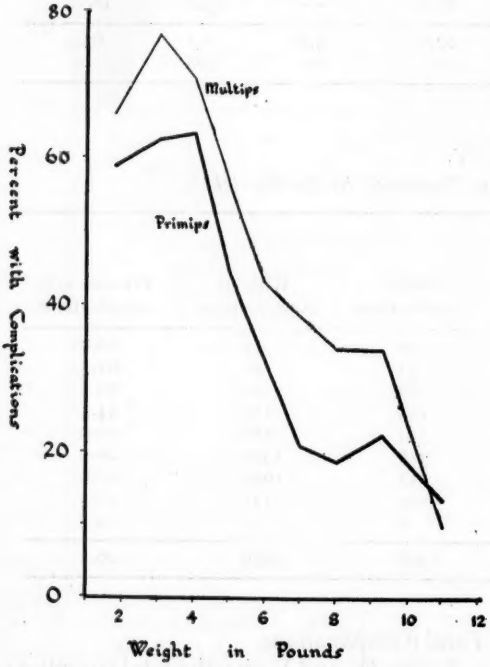

FIG. 4.

Incidence of maternal complications in relation to birth-weight.

TABLE VI.

All Primiparae: Cumulative Percentages by Birth Weights in Cases With and Without Complications of Pregnancy.

Birth-weight		With complications	Without complications
Pounds	Ounces		
Less than:			
2	9	1.5	0.4
3	9	4.1	0.9
4	9	9.3	2.0
5	9	17.3	5.6
6	9	43.6	21.6
7	9	71.1	58.5
8	9	90.4	87.9
10	1	99.9	99.7
12	1	100.0	100.0

when the mother has complications as in the control group. Table VII shows a similar picture for multiparae. Multiple births are excluded from these and subsequent tables where the different criteria of maturity applicable to twins and triplets,

TABLE VII.

All Multiparae: Cumulative Percentages by Birth Weights in Cases With and Without Complications of Pregnancy.

Birth-weight		With complications	Without complications
Pounds	Ounces		
Less than:			
2	9	2.5	0.9
3	9	6.8	1.8
4	9	14.4	4.0
5	9	21.9	8.1
6	9	41.0	25.9
7	9	70.3	58.4
8	9	89.2	84.1
10	1	99.8	98.6
12	1	100.0	100.0

and that complications in the mother tend to lower the birth-weight of their babies. The question arises whether the lower survival-rate in the group with complications is solely due to the increased proportion of smaller babies, or whether there is any adverse effect on the infant of the complication itself apart from that of diminishing its birth-weight. The necessary data are displayed in Tables VIII and IX, which show, for primiparae and multiparae respectively, the survival rates in each birth-weight group for infants born to mothers with and without complications. The survival rates do not appear to be strikingly different in the various weight-groups as when the cases with and without complications are compared, though they tend on the whole to be lower when complications are present.

A more accurate comparison may be

TABLE VIII.

All Primiparae Except Multiple Births: Percentage Surviving by Birth-weights in Cases With and Without Complications of Pregnancy.

Birth-weight				With complications		Without complications	
Pounds	Ounces		Pounds	Ounces	Number of cases	Per cent surviving	Number of cases	Per cent surviving
Below			2	9	15	0.0	10	0.0
2	9	to	3	8	30	33.3	16	18.8
3	9	to	4	8	49	55.1	28	75.0
4	9	to	5	8	79	78.5	105	81.9
5	9	to	6	8	243	94.7	548	94.9
6	9	to	7	8	338	94.7	1337	98.0
7	9	to	8	8	242	95.0	1082	98.0
8	9 and over				126	95.2	444	96.8

or other features of multiple births, would appear to affect the conclusions to be drawn.

The crude survival-rate in the group with complications is lower than in the controls. It has already been shown that chances of survival increase markedly with every half-pound rise in birth-weight, made be made by calculating the number of survivors that would be expected in the group with complications if at each weight-level they had the same chances of survival as those of corresponding weight without complications, and comparing this expected number of survivors with those actually observed. These comparisons,

for primiparae and multiparae respectively, are shown in Tables X and XI. The number of "expected" survivors is calcalculated as follows: Weight group 2 pounds 9 ounces to 3 pounds 8 ounces.

A similar calculation is made at each weight-level. A positive difference in the last column indicates that the group with complications did better than the group without complications at that weight-level;

TABLE IX.

All Multiparae Except Multiple Births: Percentage Surviving by Birth-weights in Cases With and Without Complications of Pregnancy.

Birth-weight				With complications		Without complications	
Pounds	Ounces	Pounds	Ounces	Number of cases	Per cent surviving	Number of cases	Per cent surviving
Below	2	9		23	0.0	12	0.0
2	9 to	3	8	40	20.0	11	18.2
3	9 to	4	8	70	52.9	20	65.6
4	9 to	5	8	68	76.5	44	72.7
5	9 to	6	8	145	82.8	183	92.9
6	9 to	7	8	285	94.7	498	96.4
7	9 to	8	8	204	98.0	395	96.2
8	9 and over			117	94.0	244	94.3

TABLE X.

All Primiparae Except Multiple Births: Observed and "Expected" Survivors by Birth-weights in Cases With Complications of Pregnancy.

Birth-weight					With complications			Observed minus "expected" survivors
Pounds	Ounces	Pounds	Ounces	Survival rate, no complications	Number of cases	Observed survivors	"Expected" survivors	
Below	2	9		0	15	0	0	0
2	9 to	3	8	0.1875	30	10	5.63	+4.37
3	9 to	4	8	0.7500	49	27	36.75	−9.75
4	9 to	5	8	0.8190	79	62	64.70	−2.70
Total premature					173	99	107.08	−8.08
5	9 to	6	8	0.9489	243	230	230.58	−0.58
6	9 to	7	8	0.9798	338	320	331.17	−11.17
7	9 to	8	8	0.9797	242	230	237.09	−7.09
8	9 and over			0.9685	126	120	122.03	−2.03
Total mature					949	900	920.87	−20.87

Survival-rate without complications = 0.1875.

Number of survivors "expected" in group with complications = number of cases × 0.1875 = 30 × 0.1875 = 5.63

Number of survivors observed = 10

Observed − "expected" survivors = + 4.37

a negative sign indicates that they did worse. The observed and expected survivors were summed for premature and mature infants, and the test of statistical significance described in Appendix A was applied. In all 4 groups—premature and mature primiparae (Table X), and prema-

TABLE XI.

All Multiparae Except Multiple Births: Observed and "Expected" Survivors by Birth-weights in Cases with Complications of Pregnancy.

Birth-weight				Survival rate, no complications	With complications			Observed minus "expected" survivors
Pounds	Ounces	Pounds	Ounces		Number of cases	Observed survivors	"Expected" survivors	
Below	2	9		0	23	0	0	0
2	9 to	3	8	0.1818	40	8	7.27	+0.73
3	9 to	4	8	0.6500	70	37	45.50	−8.50
4	9 to	5	8	0.7273	68	52	49.46	+2.54
Total premature					201	97	102.23	−5.23
5	9 to	6	8	0.9290	145	120	134.70	−14.70
6	9 to	7	8	0.9639	285	270	274.71	−4.71
7	9 to	8	8	0.9620	204	200	196.25	+3.75
8	9 and over			0.9426	117	110	110.28	−0.28
Total mature					751	700	715.94	−15.94

ture and mature multiparae (Table XI)—the group with complications did worse than the controls; but the differences are relatively small and statistically not significant. Detailed examination of the tables shows that, at all weight-levels except one, the first-born infants of mothers with complications did worse than the control group. Among multiparae the differences are smaller and more erratic, as would be expected, since the mothers without complications of pregnancy would usually have been admitted because of complication of delivery or some other adverse indication. Tables X and XI therefore suggest, but by no means prove, that complication of pregnancy in the mother may sometimes have a deleterious effect on the baby's chance of survival over and above the effect in depressing the birth-weight. The possibility at once suggests itself that the effect will vary with the nature of the complication. Some kinds of complication may have a big effect on the infant, others none at all. So far all complications have been grouped together. It is now necessary to consider them separately:—

A. *Complication of the Pregnancy Itself.*

The following complications of the pregnancy itself were recorded on the individual code cards:—

1. Pre-eclamptic toxaemia including hypertension. The latter condition was included in this group because the case notes by no means always made it clear whether the condition described was one of pre-eclamptic toxaemia or essential hypertension, especially when the woman was first seen late in pregnancy. In any case, the number of women with hypertension was very small compared with those with toxaemia.

This group was sub-divided into those cases specifically referred to as "mild" and the remainder. A separate class-heading was used for cases having an ante-partum haemorrhage as well as toxaemia.

2. Eclampsia, ante- or intra-partum.

3. Hyperemesis, of sufficient severity to necessitate treatment in hospital.

4. Antepartum haemorrhage, comprising placenta praevia or separation of the placenta from any other cause, except cases associated with toxaemia. It was impos-

sible from the case notes to be certain in every instance whether the antepartum haemorrhage was due to a misplaced placenta or to some other cause. All cases of antepartum haemorrhage have been listed together. Cases of slight bleeding in the latter half of pregnancy, or of prolongation of the menses in early pregnancy, were not included.

5. Pyelitis of pregnancy.
6. Hydramnios.

Table XII shows the proportion of these complications occurring in booked married primiparae, which gives a fair indication of their incidence in the population at large. The percentage among unbooked cases and multiparae is considerably higher, as many of these mothers were admitted because of these complications.

The relation between these complications in primiparae and the birth-weight of the infants is shown in Table XIII. This table gives the cumulative percentages by weight of infants born to mothers having the specified complication. The data in this table are set out in diagrammatic form in Fig. 5. In uncomplicated pregnancies, 0.7 per cent of the infants are $3\frac{1}{2}$ pounds or less,

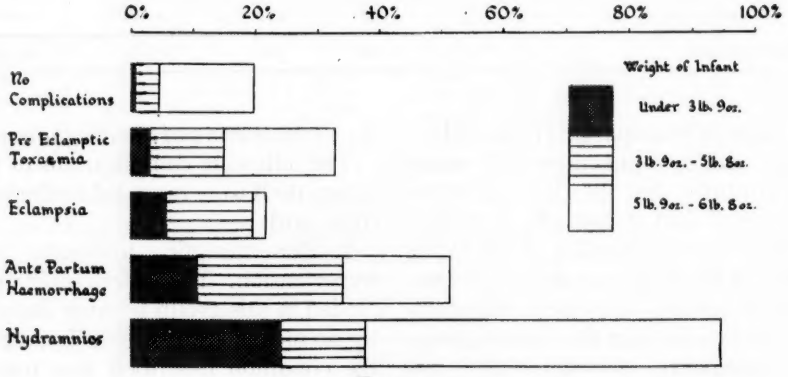

FIG. 5.
Birth-weights in absence and presence of maternal complications.

TABLE XII.
Complications of Pregnancy in Booked Married Primiparae.

Complication	Number of cases	Rate per 100 pregnancies
Pre-eclamptic toxaemia	532	14.0
Mild	232	6.1
Moderate and severe	300	7.9
Pre-eclamptic toxaemia with antepartum haemorrhage	4	0.1
Eclampsia	33	0.9
Hyperemesis	17	0.4
Antepartum haemorrhage	31	0.8
Pyelitis	41	0.4
Hydramnios	22	0.6
Total	680	17.2

4.5 per cent are premature, and 19.8 per cent are $6\frac{1}{2}$ pounds or less. In cases with complications these rates are much higher, the prematurity-rate, for example, ranging from 14.9 per cent for pre-eclamptic toxaemia to 34.3 per cent for antepartum haemorrhage and 37.8 per cent for hydramnios.

Table XIII also shows, for each specific complication, the excess in the prematurity-rate as compared with the control group without complications, the standard deviation of this excess (calculated as described in Appendix A) and t, the ratio of the difference to its standard deviation. According

TABLE XIII.

All Primiparae Except Multiple Births: Cumulative percentages by Birth-weight in Cases With and Without Complications of Pregnancy.

Birth-weight		Without complications	Pre-eclamptic toxaemia	Eclampsia	All toxaemias	Pre-eclamptic toxaemia plus antepartum haemorrhage	Antepartum haemorrhage	Hydramnios
Pounds	Ounces							
Below 2	9	0.3	0.8	2.0	0.8	0.0	5.3	10.8
3	9	0.7	3.2	5.9	3.2	9.5	10.7	24.3
4	9	1.5	7.0	11.8	7.3	23.8	27.7	35.1
5	9	4.5	14.9	19.6	15.6	42.9	34.3	37.8
6	9	19.8	33.1	21.6	32.0	47.6	51.4	94.5
12	1	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Number of cases		3570	631	51	709	21	76	37
Excess per cent premature			10.3	15.1	11.1	38.4	29.8	33.3
Standard deviation of difference			2.18	9.08	2.13	22.22	10.15	12.56
t			4.83	1.66	5.26	1.73	2.93	2.66

TABLE XIV.

All Multiparae Except Multiple Births: Cumulative Percentages by Birth-weight in Cases With and Without Complications of Pregnancy.

Birth-weight		Without complications	Pre-eclamptic toxaemia	Eclampsia	All toxaemias	Pre-eclamptic toxaemia plus antepartum haemorrhage	Antepartum haemorrhage	Hydramnios
Pounds	Ounces							
Below 2	9	0.9	1.6	0.0	1.5	4.8	6.3	4.2
3	9	1.6	4.3	5.9	5.9	4.8	16.6	33.4
4	9	3.1	10.2	29.4	10.9	23.8	33.8	41.7
5	9	6.2	18.4	35.3	19.4	38.1	44.2	45.9
6	9	19.2	36.2	94.1	38.8	95.3	56.2	91.7
12	1	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Number of cases		1407	439	17	459	21	174	24
Excess per cent premature			12.2	29.1	13.2	31.9	38.0	39.7
Standard deviation of difference			3.08	23.28	3.11	20.30	7.84	20.79
t			3.98	1.25	4.24	1.57	4.86	1.91

to the usual statistical convention, where t is 2 or more the difference may be regarded as significant. This is found to be true in all complications except eclampsia and pre-eclamptic toxaemia plus antepartum haemorrhage, in which two categories the number of cases was very small. However, even in these groups, t is greater than 1.65, so the odds are at least 20 to 1 against a difference as great as that observed occurring by chance in the expected direction. The reality of the effect is further emphasized by the significant result obtained with the less severe forms of toxaemia, where many more cases are available. It may, therefore, be concluded that all these types of complication of pregnancy have a significant and marked effect in decreasing the birth-weight of infants born to primiparae. Table XIV shows that the same conclusions apply to multiparae.

The next question that arises is whether any or all of these complications exercise an adverse effect on the foetus apart from that on its birth-weight. This can be best answered by applying the method of "expected survivors," already applied in Tables X and XI to the total complication group. Table XV shows the results for cases of toxaemia, antepartum haemorrhage and hydramnios in primiparae and multiparae. In each case the standard deviation is shown (calculated as described in Appendix A) and t, the ratio of the difference between observed and "expected" survivors and the standard deviation of the difference.

For the group of all toxaemias, the differences are not all of the same sign. Premature infants, both in primiparae and multiparae, appear to do very slightly better than the controls, whereas the mature babies do worse. But none of the differences are significant, the values of t being 0.30, 0.33, 1.31, and 1.74. The differences between observed and expected survivors, taken as a whole, are no greater than would be expected from chance sampling variation. While toxaemias of pregnancy, as already shown, have a marked and significant effect in lowering the birth-weight of the infant, there is no reason to suppose that they have any other consequence that can be measured by means of survival rates.

In antepartum haemorrhage the 4 differences are all in the same direction. In every case the babies in the group with complications do worse than the controls. The differences among the premature babies are both significant, even when considered in isolation, having t values of 2.61 and 2.11. The difference for mature infants do not reach the level of statistical significance when taken individually; but the fact that they are all in the same direction strengthens the case for regarding the whole evidence as affording a very good reason indeed for concluding that the babies born of mothers with antepartum haemorrhage have a greater risk of death than their weight alone would indicate. In the third paper in this series it will be shown that death or stillbirth due to asphyxia is a common finding in cases of antepartum haemorrhage. In hydramnios, as in antepartum haemorrhage, all 4 differences are in the same direction, showing that hydramnios in the mother lessens the chance of survival in the foetus. The 2 differences for premature infants are highly significant, with t values of 7.77 and 4.01 while the differences for mature infants have t values of 1.14 and 0.80. The probability of all 4 differences in the same direction occurring by chance is very small indeed. It can be concluded that hydramnios in the mother, like antepartum haemorrhage, not only tends to induce premature labour, but also has other harmful effects on the foetus. These are more marked in hydramnios than in antepartum haemorrhage. Indeed,

TABLE XV.

Observed and "Expected" Survivors in Specified Complications.

Complications		Premature					Mature				
		Observed survivors	Expected survivors	Difference	Standard deviation difference	t	Observed survivors	Expected survivors	Difference	Standard deviation difference	t
Toxaemias:	Primiparae	75	73.26	+1.74	5.81	0.30	570	581.47	−11.47	6.58	1.74
	Multiparae	58	50.22	+7.78	5.92	1.31	350	352.07	−2.07	6.27	0.33
A. P. H.	Primiparae	8	14.60	−6.60	2.52	2.61	40	48.53	−8.53	9.27	0.92
	Multiparae	24	35.86	−11.86	5.62	2.11	80	92.37	−12.37	9.50	1.30
Hydramnios:	Primiparae	0	4.76	−4.76	0.61	7.77	20	21.89	−1.89	1.66	1.14
	Multiparae	0	4.13	−4.13	1.03	4.01	20	22.02	−2.02	2.53	0.80

TABLE XVII.

All Single Births: Cumulative Percentages by Birth-weight in Cases with Chronic Maternal Disease.

Birth-weight			No complications	All chronic disease	Cardiac disease	Pulmonary tuberculosis	Chronic chest disease	Acquired syphilis	Diabetes	Anaemia	Local disease of uterus
	Pounds	Ounces									
Below	2	9	0.4	1.1	0.6	0.0	1.8	0.0	0.0	3.2	0.0
	3	9	1.0	2.7	1.7	0.0	5.5	1.8	0.0	3.2	0.0
	4	9	1.9	5.9	3.4	6.1	5.5	6.1	33.3	6.3	11.8
	5	9	4.9	10.2	6.3	9.1	9.1	9.6	50.0	11.3	29.4
	6	9	19.6	34.9	41.7	9.1	27.3	20.2	50.0	14.5	94.1
	12	1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
No. of cases			4977	557	175	33	55	114	6	62	17
Excess per cent premature				5.3	1.4	4.2	4.2	4.7	45.1	6.4	24.5
Standard deviation of difference				1.93	2.32	7.30	5.50	3.85	20.40	5.59	20.30
t				3.12	0.47	0.57	0.76	1.22	2.21	1.14	1.21

no premature infants in the hydramnios group survived. The high wastage rate associated with hydramnios is largely due to the frequent occurrence of congenital defects, especially anencephalus.

B. *Acute Infection and Injuries.*

Acute infections and injuries were recorded if they occurred within 3 months of delivery. Only those conditions serious enough to be treated in hospital were included, because of the likelihood that milder conditions might not have been mentioned in many of the case notes, especially where the pregnancy and delivery were straightforward. The 71 cases included influenza, pneumonia, subacute bacterial endocarditis, acute gonorrhoea, thrombophlebitis, ischiorectal abscess, acute appendicitis, intussusception, fractures, and severe falls without fracture. Table XVI shows the percentage of premature infants born to mothers with the

TABLE XVI.

Infants Whose Mothers had Acute Infections and Injuries.

	Pre-mature	Per cent survivors	
	Per cent	Pre-mature	Mature
Mothers with acute infections and injuries	11.3	62.5	95.2
Mothers without complications	4.9	63.8	96.8

above conditions, as well as the survival rates for premature and mature babies. As might be expected, the prematurity rate is higher than in the control group. There is no evidence of any adverse effect on the infant apart from that on its birth-weight. The numbers of cases in the various diagnostic categories are too small to allow of the sub-division of the group into its individual infections and injuries.

C. *Chronic Maternal Diseases.*

Among all the primiparae and multiparae, excluding cases of multiple birth, there were 557 records of chronic conditions in the mother coincident with pregnancy, distributed as follows: —

Cardiac disease	175
Pulmonary tuberculosis	33
Chronic chest diseases (except tuberculosis)	55
Diabetes	6
Syphilis (acquired)	114
Syphilis (congenital)	32
Anaemia	62
Local disease of uterus or ovaries	17
Others	63

The term anaemia covers cases of hypochromic anaemia with a haemoglobin percentage of 50 or less, and cases of pernicious anaemia, the former being by far the more frequent. Table XVII gives cumulative percentages by weight of infants born to mothers with these diseases. The prematurity-rate for all chronic diseases is 10.2 per cent compared with the control figure of 4.9 per cent and the difference, 5.3 per cent with a t value of 3.12, is statistically significant. In each of the chronic conditions listed the prematurity-rate is increased, though not very strikingly except in diabetes and local uterine disease. In no individual group is the difference statistically significant by itself, the value of t never rising above 1.22 except in diabetes, where a t value of 2.21, based on only 6 cases, does not correspond to the conventional odds of at least 1 in 20. Nevertheless, taken all together, there is strong evidence that chronic complications have an adverse effect on the birth-weight of the infant. But the effect is not so well established, nor anything like so important quantitatively, as that observed with complications of the pregnancy itself, such as toxaemia and antepartum haemorrhage. The method of " expected survivors " was applied to the 2 largest groups, cardiac disease and acquired syphilis, to test

whether there was any adverse effect on the foetus part from that on weight. No significant difference was found between the observed and the expected numbers of survivors.

Comparison with Results of Other Workers.

All authorities are agreed as to the importance of pathological conditions in the mother acting on the infant, but opinions differ widely as to the relative prominence of the various specific complications. In most cases the results are based upon analysis of records of premature infants, or of stillbirths or deaths, without any control groups, nor is there usually any differentiation by booked and emergency admissions, primiparity and multiparity, or any clear indication of the composition of the hospital sample in relation to the general population.

Anderson, Brown and Lyon (1941) in a controlled survey of a year's births in Cincinnati General Hospital, give toxaemia, uterine bleeding and syphilis as the most important complications leading to prematurity. Diddle and Plass (1942) also specify toxaemias and syphilis as being of major importance. Tyson (1934) attributed 18 per cent of 469 premature births to syphilis, this being responsible for more premature births than any other single complication.

Most of the American authors are agreed on the importance of syphilis in the aetiology of prematurity, stillbirths and infant deaths. This is not found in the present series of cases. The prematurity-rate in syphilis, though higher than where no complications occurred, is not markedly so; and the number of cases are relatively few. In a later paper it will be shown that congenital syphilis is a comparatively unimportant cause of stillbirth and neonatal death. These results pay tribute to the good effect of the antenatal treatment which nearly all the cases received. The importance attributed to syphilis by American investigators may be partly due to the frequency of the condition among negro mothers, who have, in any case, a higher prematurity-rate than the white population. Dunham (1939), in New Haven, U.S.A., found that the average birth-weight of white infants, as compared with negroes, was 175 g. higher in males and 337 g. in females.

The effect of maternal complications on the foetus, other than on the birth-weight, has been investigated by Breese (1938). He calculated observed and expected wastage-rates for a number of complications, which he expressed as percentages by a method essentially similar to that used in this paper. His findings were as follows:

	Observed mortality per cent	Expected mortality per cent
Pre-eclamptic toxaemia	27	26
Threatened abortion	75	67
Bleeding	65	63
Placenta praevia	46	35
Hydramnios	100	60
Syphilis	24	17
Cardiac disease	40	43

The difference between observed and expected mortality was significant only in the case of hydramnios.

Factors Affecting Birth-weight.

2. Age of Mother.

Table XVIII shows the percentage of infants at or below certain weight levels born to primiparous mothers in different age groups. The prematurity-rate is seen to rise with increasing age of mothers, especially after the age of 30 years. This table refers to all firstborn infants, excluding multiple births, as the incidence of twins and triplets is known to go up with maternal age.

TABLE XVIII.

All Primiparae Except Multiple Births: Cumulative Birth-weight Percentages by Age of Mother.

Birth-weight		Age of mother in years					
Pounds	Ounces	15–19	20–24	25–29	30–34	35–39	40–44
Below 2	9	0.0	0.5	0.6	0.4	1.4	0.0
3	9	1.1	1.2	1.4	2.5	2.9	7.4
4	9	2.2	2.4	2.9	6.8	7.2	7.4
5	9	5.3	5.9	5.9	13.2	15.9	18.5
6	9	22.9	20.2	25.5	32.6	37.0	22.2
7	9	72.1	57.2	56.5	67.1	63.0	100.0
8	9	91.6	89.1	84.1	90.3	85.1	
10	1	100.0	99.9	99.2	99.6	99.5	
12	1		100.0	100.0	100.0	100.0	
Number of cases		358	2259	1359	484	208	27

Maternal age and Incidence of Complications.

In previous sections the prematurity-rate has been shown to be positively associated with complications in the mother. The relation between complication-rates and age of mother was therefore investigated. Table XIX shows percentage complication-incidence by age of mother in all primiparae, excluding multiple births. The complication-rate is seen to rise with maternal age, this being largely due to increase in the incidence of toxaemias. Chronic medical diseases, as might be expected, are also more frequent in the older mothers. The slight fall in complications after the age of 35 is based upon small numbers, and is not significant. The figures for booked primiparae only gave a smaller proportion of complications in all age groups, as would be expected, but showed similar trends for toxaemias and chronic disease.

TABLE XIX.

All Primiparae Except Multiple Births: Percentage Complications by Age of Mother.

	Age of mother in years				
	15–19	20–24	25–29	30–34	35 and over
No complications	89.1	80.2	69.7	64.9	78.3
All complications	10.9	19.8	30.3	35.1	21.7
All toxaemias	4.2	12.9	20.5	21.6	16.2
Antepartum haemorrhage ...	3.1	1.0	0.5	3.5	2.1
Hydramnios	0.6	0.4	0.9	0.2	0.9
Chronic medical diseases ...	2.8	4.4	8.4	7.3	2.6
Others	0.3	1.1	0.1	2.4	0.0
Total cases	358	2259	1358	482	235

Maternal Age and Toxaemias.

Two questions now arise:—

1. Is the rise in prematurity-rate with age due partly or entirely to the increasing incidence of toxaemias?

2. Given a mother with toxaemia, has age any effect on her chance of producing a premature baby?

Table XX sets out prematurity-rates by age of mother, sub-divided into those with with toxaemia (Column A), those without

toxaemia (Column B), and the total group (Column C). The prematurity-rate is seen to rise with age after 30 years in both the toxaemic and the non-toxaemic mothers. The effect of age of mother on the prematurity-rate cannot therefore be solely attributed to toxaemias. Column D shows that the ratio of the prematurity-rates for toxaemic and non-toxaemic mothers, at any given age-level, is approximately constant at about 2½. The figure of 4.3 for the 15 to 19 age-group is based on only 3 premature infants, and so does not differ significantly from the value at the other ages.

TABLE XX.

All Primiparae Except Multiple Births: Prematurity Rate by Age in Mothers With and Without Toxaemia.

Age of mother	Column A: Per cent premature mothers with toxaemia	Column B: Per cent premature mothers without toxaemia	Column C: Per cent premature all mothers	Column D: Ratio A/B
15 to 19	20.0	4.7	5.3	4.3
20 to 24	12.0	5.0	5.9	2.4
25 to 29	11.9	4.4	5.9	2.7
30 to 34	24.0	9.8	13.2	2.5
35 and over	31.6	13.2	16.2	2.4

TABLE XXI.

All Primiparae Except Multiple Births: Outcome by Maternal Age.

Age of mother	Premature: Per cent lived	Premature: Per cent died	Premature: Per cent stillborn	Full time: Per cent lived	Full time: Per cent died	Full time: Per cent stillborn
Under 20	60.9	26.1	13.0	97.4	1.5	1.1
20 to 34	66.4	14.7	18.9	97.1	0.8	2.1
Over 34	63.8	14.9	21.3	92.4	1.3	6.3

Outcome by Age of Mother.

Table XXI shows the outcome for premature and mature infants by age of mother. Stillbirth-rates rise steadily with age. This is in agreement with the experience for the country as a whole, as shown, for example, in the figures calculated by Woolf (1946) from the data for 1939–40 in the Annual Reviews of the Registrar-General for England and Wales. The stillbirth-rates for primiparae rose steadily with age of mother, from 27 per 1,000 in the 15 to 19 age-group to 113 in those between 40 and 45 years. Neonatal death-rates are high in very young and very old mothers. This also is in accord with general experience, for example in the survey conducted by Woodbury (1925).

FACTORS AFFECTING BIRTH-WEIGHT.

3. LEGITIMACY.

Among the primiparae studied, 495 were unmarried. The number of unmarried multiparae was too small to allow of any valid comparison to be made with the corresponding married group, especially as the majority of unmarried mothers gained admission on this ground alone, whereas the married women usually had some complication. The present section therefore deals with primiparae only.

The distributions of weight of legitimate and illegitimate first births, excluding multiple births, are shown in Table XXII. Among the illegitimate 8.1 per cent were premature, compared with 6.9 per cent among the legitimate babies. It has already been shown that complication-rates and maternal age have an important bearing on the weight of the infant. Both these factors must therefore be examined.

TABLE XXII.

Birth-weight Percentages in Unmarried and Married Primiparae Excluding Multiple Births.

Birth-weight				Unmarried mothers		Married mothers	
Pounds	Ounces	Pounds	Ounces	Per cent	Cumulative per cent	Per cent	Cumulative per cent
	Below	3	9	1.2	1.2	1.5	1.5
3	9 to	5	8	6.9	8.1	5.4	6.9
	Over	5	8	91.9	100.0	93.1	100.0

Complication-Rates.

Unmarried mothers were found to have a total complication-rate of 19.4 per cent, being 5 per cent lower than that of the married group. This is entirely due to the low toxaemia rate of 8.7, which is just over half that of the married women (15.9 per cent). This is probably due to the younger age-composition of the unmarried mothers, and to the higher proportion in the unbooked cases admitted for social reasons rather than complications. The incidence of antepartum haemorrhage is over twice as high in the unmarried group, being 3.2 per cent as compared with the married rate of 1.4 per cent. This is possibly due to a higher incidence of mechanical interference in this group.

Age of Mother.

The average age of the unmarried mothers was 26.2 years, compared with 28.1 years for the married. Table XXIII shows the percentage of premature babies born to married and to unmarried mothers under the age and over the age of 25 years. For the younger women, the prematurity-rate is the same in 2 groups; but at ages 25 and over, unmarried mothers have an excess of 5.9 per cent over the married. The difference is not statistically significant, but the *t* value of 1.29 indicates that a deviation as great as this would not happen by chance more than once in 10 trials. This high prematurity-rate in the older unmarried mothers may be associated with the fact that they have often a considerably harder time than the younger girls. The young girl is more often accepted back into the family circle, and preference is all given to younger girls for admission to homes for the unmarried.

TABLE XXIII.

Percentage Premature Married and Unmarried Primiparae Excluding Multiple Births.

	Mothers under 25	Mothers 25 and over
	Per cent	Per cent
Married mothers	5.8	8.3
Unmarried mothers	5.8	14.2
Difference		5.9
Standard deviation		4.57
t		1.29

Prematurity-rate. Allowing for Age and Complications.

From their lower complication-rate and younger age-composition, one would expect the unmarried mothers to have a lesser incidence of prematurity than the mar-

ried, rather than the greater rate actually observed. Table XXIV shows the calculation of the number of premature babies that would be expected in the unmarried group, if at each age and complition-level they had the same chance of 6.5919 per cent. Similarly, considering complications alone, the lower incidence among the unmarried would lead to a prematurity-rate of 6.7779 per cent. When both these favourable influences are taken into account, the expected prematurity-

TABLE XXIV.

All Primiparae Except Multiple Births: Comparison of Premature Rates in Married and Unmarried Mothers, Allowing for Age and Complications.

(*a*) *Allowance For Age Differences*

Age of mother	Married mothers, per cent premature	Unmarried mothers, total	Number of prematures expected
15 to 19	5.38	98	5.27
20 to 24	5.84	263	15.36
25 to 29	5.79	78	4.52
30 to 34	12.91	30	3.87
35 to 39	13.97	25	3.49
40 to 44	12.12	1	0.12
Totals		495	32.63
Percentage of prematures expected			6.5919

(*b*) *Allowance for Differences in Incidence of Complications*

Complication	Married mothers, per cent premature	Unmarried mothers, total	Number of prematures expected
Toxaemias	14.86	43	6.39
Antepartum haemorrhage	35.00	16	5.60
Others	11.04	37	4.08
None	4.38	399	17.48
Totals		495	33.55
Percentage of prematures expected			6.7779

(*c*) *Method of Calculation.*

Percentage of prematures in married group ... ... = 6.9573

Expected percentage of prematures in unmarried group after allowing for age and complication differences $= \frac{6.5919 \times 6.7779}{6.9573}$

$= 6.4219$

Expected number of prematures ... ... = 6.4219 per cent of 495

$= 31.8$

Observed number of prematures ... ... = 40.0

Excess ... ... = 8.2

bearing premature infants as obtains in the married mothers. The actual prematurity-rate among the married women was 6.9573 per cent. If allowance is made for age only, the more favourable age composition of the unmarried women would lead one to expect a lower prematurity-rate, namely rate is 6.4219 per cent, giving an expected number of premature infants of 31.8, against the 40 actually observed. The excess of 8.2 prematures among the unmarried mothers must be due to causes other than age or complications.

The difference is not statistically signifi-

cant, being only just above its standard deviation. It is nevertheless suggestive, when considered in connexion with the observations of other workers such as Toverud (1933), who discussed the effect of illegitimacy on the weight and maturity of the infant, using as his material cases admitted to a home for unmarried mothers in Oslo. Over a period of 2 years the inmates received systematic prenatal care and an optimum diet. It was found that mothers admitted 2 months or more before delivery had larger babies than those admitted for 6 weeks or less, and those again had heavier infants than mothers admitted just before delivery. The average birth-weights in the 3 groups were 3,587 g., 3,347 g., and 3,240 g., giving a difference between the first and third groups of about three-quarters of a pound.

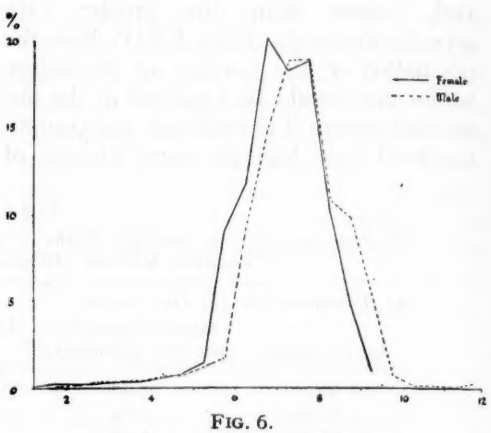

FIG. 6.
Distribution of birth-weight by sex.

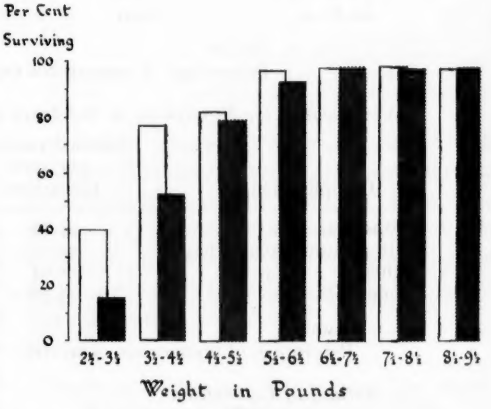

FIG. 7.
Survival-rates according to sex of infant.
Outlined rectangles—Females.
Black rectangles—Males.

FACTORS AFFECTING BIRTH-WEIGHT.

4. SEX.

Fig. 6 shows the percentage distribution of male and female primiparous births according to weight. If one takes the usual limit of prematurity—5 pounds 8 ounces or less—6.7 per cent of the firstborn male babies would be classed as premature, and 7.5 per cent of the females, a difference of 0.8 per cent. Among the multiparae, the figures are 10.7 per cent for the males and 13 per cent for the females with a difference of 2.3 per cent. At weights of 6½ pounds or less, the excess for females among firstborn is 10.3 per cent, and 14.2 per cent for multiparae. It would probably be more accurate to adopt a different weight standard of prematurity for male and female infants, since female infants of the same gestation time would certainly tend on the average to be lighter than male babies. This is, however, a matter for general agreement. In this paper, the standard criterion will be adhered to.

Outcome of Sex and Weight.

Tables XXV and XXVI give comparative figures of outcome by birth-weight in male and female infants. The data for survival-rates given in Table XXV, which relate to primiparae, excluding multiple births, are shown in Fig 7. Girl babies have a much higher survival-rate among the premature and smaller mature-weight groups. This is due to the decreased wastage from deaths. The death-rate for

male firstborn premature infants was 23.8 as compared with 6.1 per cent for female. Among multiparae the rates were 25 per cent for males and 14.8 per cent for females. The stillbirth-rate was slightly higher than the male in firstborn premature infants, and about the same in the multiparae.

In a later paper, male and female death-rates by pathological cause will be compared.

TABLE XXV.

Primiparae Except Multiple Births: Outcome by Weight and Sex.

Birth-weight				Male infants			Female infants		
Pounds	Ounces	Pounds	Ounces	Per cent lived	Per cent died	Per cent stillborn	Per cent lived	Per cent died	Per cent stillborn
	Below	2	9	0.0	62.5	37.5	0.0	20.0	80.0
2	9 to	3	8	15.4	50.0	34.6	40.0	5.0	55.0
3	9 to	4	8	52.5	27.5	20.0	77.1	0.0	22.9
4	9 to	5	8	79.1	10.5	10.5	81.7	6.5	11.8
5	9 to	6	8	92.2	3.8	4.0	96.2	1.1	2.7
6	9 to	7	8	97.3	0.5	2.2	97.2	1.0	1.8
7	9 to	8	8	97.1	0.4	2.5	97.7	0.7	1.6
8	9 to	10	0	97.3	1.0	1.7	97.2	0.0	2.8
10	1 and over			66.7	0.0	33.3			

TABLE XXVI.

Multiparae Except Multiple Births: Outcome by Weight and Sex.

Birth-weight				Male infants			Female infants		
Pounds	Ounces	Pounds	Ounces	Per cent lived	Per cent died	Per cent stillborn	Per cent lived	Per cent died	Per cent stillborn
	Below	2	9	0.0	46.2	53.8	0.0	26.3	73.7
2	9 to	3	8	10.5	42.1	47.4	26.7	26.7	46.6
3	9 to	4	8	45.3	24.5	30.2	68.6	14.3	17.1
4	9 to	5	8	70.2	12.8	17.0	81.0	5.2	13.8
5	9 to	6	8	76.9	8.7	14.4	93.7	0.5	5.8
6	9 to	7	8	94.4	1.2	4.4	97.1	1.1	1.7
7	9 to	8	8	96.9	0.5	2.6	96.5	0.0	3.5
8	9 to	10	0	94.7	0.0	5.3	97.1	0.0	2.9
10	1 and over			90.9	0.0	9.1			

SUMMARY.

A statistical analysis has been made of nearly 8,000 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive.

Prematurity rates. The prematurity-rate among all primiparae was 8.6 per cent, and 5.9 per cent when emergency cases, illegitimate births and multiple births were excluded.

Outcome and birth-weight. Outcome—whether the infant was stillborn, died or survived—was closely related to birth-weight, wastage decreasing from 100 per cent for babies under 2 pounds 9 ounces to about 3 per cent for babies over 6 pounds, with a rise for postmature births. In the smallest babies stillbirths constituted about half the total wastage, the proportion rising to 80 per cent for mature and 100 per cent for postmature infants.

Complications of pregnancy. The prematurity-rate among mothers with complications was 3 times as high as among those

without complications. In complications of the pregnancy itself, the prematurity-rates were: toxaemias, 15.6 per cent; antepartum haemorrhage, 34.3 per cent; hydramnios, 37.8 per cent. In mothers without complications the rate was 4.5 per cent. The most common chronic diseases coincident with pregnancy were cardiac disease, syphilis and anaemia. For mothers with chronic conditions the prematurity-rate was 10.2 per cent. Chronic medical diseases are far less important causes of prematurity than complications of pregnancy itself.

The increased mortality of babies of mothers with toxaemia and chronic medical disease is entirely accounted for by the decrease in birth-weight, but babies of mothers with antepartum haemorrhage and hydramnios have an extra risk when the effect of reduced weight is taken into account.

Age of mother. Prematurity-rates increase with age of mother. This is partly due to increased incidence of toxaemias. Stillbirth-rates also rise with maternal age but neonatal death-rates are higher in the younger and older age-groups.

Legitimacy. Illegitimate babies had a higher prematurity-rate than the legitimate, accounted for by an increase in the group of older unmarried mothers.

Sex. Girl babies on the whole are smaller than boys at birth, but have a lower death-rate. Stillbirth-rates were approximately the same in the two sexes.

It is a pleasure to thank Professor C. McNeil and Mr. W. F. T. Haultain for permission to use paediatric and obstetrical records; Mrs. W. Lord, B.A., and Miss Joyce Thomson for assistance in the analyses and computations; Dr. Barnet Woolf for advice on the planning of the investigation and on the statistical methods used; and Professor McNeil and Professor R. W. B. Ellis for their interest and encouragement.

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APPENDIX A.

STATISTICAL METHODS.

The variance of a percentage, p, based on a total sample $= n$, was calculated by the usual formula, $V_p = p(100-p)/n$.

The variance of the difference between two percentages is the sum of the variances of the individual percentages, and the standard deviation of the difference is the square root of this figure.

In many of the percentages and the "expected numbers", part of the births, namely those of the mature infants who survived, were sampled on a 1 in 10 basis. It is necessary to allow for this in calculating variances. Suppose the data on which the calculation rests to be as follows:

	Full sample	1 in 10 sample
" Successes "	a	b
" Failures "	c	d

Let the percentage of of successes be p, so that $p = 100(a + 10b)/(a + 10b + c + 10d)$. Then the variance of the observed number, $(a+10b)$, is

$$\frac{(a+10b)^2\ (c+100d)\ +\ (c+10d)^2\ (a+100b)}{(a+10b+c+10d)^2}$$

And the variance of p is

$$\frac{p^2\ (c+100d)\ +\ (100-p)^2\ (a+100b)}{(a+10b+c+10d)^2}$$

The variance of the difference between the observed and the " expected " number in a composite of various independent groups, such as birth-weight groups, is the sum of the variances of the individual observed and " expected " numbers in each of the groups. The variance of the observed number, in cases where the sampling is full, is $p.q\ (p+q-1)$ where p = number of " successes " and q = number of " failures ".

The variance of the " expected " number is the variance of the expected rate multiplied by $(p+q)^2$, the formula for the variance of the expected rate being $z(1-z)/(n-1)$, where z= proportion of successes in control group and n = number of cases in control group.

When the observed and expected figures are based on data of which part are sampled on a 1 in 10 basis, the formula for the variance of the observed number is

$$\frac{(a+10b)^2\ (c+100d)\ +\ (c+10d)^2\ (a+100b)}{A^2+B-2AC/B}$$

where a, b, c and d have the meanings specified above, and

$$A=a+c+10(b+d)$$
$$B=a+c+100(b+d)$$
$$C=a+c+1000(b+d)$$

The variance of the " expected " number is the variance of the expected rate multiplied by A^2, the variance of the expected rate being calculated from the data in the control group using the last formula given above, but made to apply to the rate by dividing the result by the square of the number in the control sample corresponding to A in the sample being standardized.

The derivation of the above formulae is in course of publication.

B. Woolf.

The Influence of Semen on the Female Reproductive Organs

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OUR experiments were started in 1942. They were based upon the clinical experience of one of us (G.-A.) who had observed that the uterus and upper third of vagina of many young virginal women at the time of marriage was abnormally small. Such uteri grew however to their accredited normal size within a few months of married life provided no contraceptives were used which interfered with the absorption of semen from the vagina. *Per sequitur* if sheath or withdrawal methods of contraception were employed such uterine development did not take place. Following the dictum of William Harvey to seek and search out the secrets of nature by way of experiment, the purpose of our research was to discover any scientific explanation for this observation, that is, does absorption of semen produce any effect upon the genitalia.

Preliminary experiments were carried out using semen kindly supplied by Dr. Scott Wilson of the Harley Street Laboratories. At that time no special attention was paid to the nature of the specimens proffered. Some were several days old and therefore infected or biochemically altered. Others were defective as regards the number and quality of spermatozoa present. Despite this, results were encouraging. It is necessary to refer briefly to these experiments (Green-Armytage, 1943) because they represent the basis on which further investigations have rested and have guided the plan of the later research.

It is generally agreed that if female litter mates have been and are being kept under identical conditions their reproductive organs are equally developed and are of the same length and width. Therefore in order to obtain a reliable measure for assessing the results of treatment, we have used only does of the same litter in any of these experiments, keeping one of each litter as a control and comparing our findings in the animals subjected to treatment with those of their respective untreated sisters.

Experiment 1. A 10-weeks-old rabbit doe was injected with 1 ml. of human semen on 3 consecutive days. Twenty-four hours after the last injection this animal and its control litter mate were killed by air embolism. The ovaries of the injected rabbit were large and showed some distinct *Blutpunkte* and on histological section there were numerous large follicles, some of which were haemorrhagic. Its uterus, as compared with that of the control, had increased in length and width, its lumen was filled with mucus; on microscopical examination the uterine muscular coat appeared to have thickened and its mucosa was oedematous.

Experiment 2 was a repetition of No. 1, but yielded a negative result.

Experiments 3 and 4. Two litters (a and b), one comprising 2, the other 3, female rabbits were spayed when 14 weeks old. Three weeks later, keeping one doe of each litter as a control, the rest were given 8 injections of 1 ml. human semen intravenously within the next 19 days. On the 20th day all the animals were killed. The uteri of the injected doe of litter (a) and of 1 doe of litter (b) were dark red and markedly larger than those of their respective controls. Their lumina were

filled with a mucoid mass and sections revealed increased width of the muscular coat with oedema and hyperaemia of the mucosa. The third rabbit of litter (b), although injected in the same way as its litter mate, showed a poor response, its uterus being somewhat longer but hardly thicker than that of the control. There was also no histological evidence of any effect on the uterine muscle or mucosa.

Experiment 5. A litter of 3 female rats, 6 weeks old, was used. Two animals received daily intraperitoneal injections, one of 0.2 ml., the other of 0.4 ml. of human semen. On the third morning the first was found dead, whereas the vagina of the other had opened and a smear of its mucoid contents revealed the presence of epithelial cells. Twenty-four hours later leucocytes were prevailing. On the 5th day (105 hours after the first injection) the experiment was terminated. The ovaries and the uterus of the rat which had been injected were larger than the respective organs of the control. The uterus and vagina were filled with mucus. Histology of the ovaries showed the presence of numerous ripe and maturing follicles.

Experiments 6, 7, and 8 were carried out with litters of immature rats which were spayed 5, 7 and 14 days respectively before the first injection.

Experiment 7 yielded a negative result.

In experiment 6, vaginal opening occurred in one rat after the 5th, in the second after the 7th, injection but no oestrous response was observed in any of the vaginal smears which revealed only the presence of large epithelial cells in a mucoid stringy mass. Twenty-four hours after the 10th injection of 0.4 ml. of human semen both rats together with their untreated litter mate were killed. The uteri of the injected animals had markedly increased in length and width in comparison with the uterus of the control.

In experiment 8, vaginal opening was observed in all 3 injected rats after the 6th injection. Only dioestrous response was obtained. At autopsy uteri and vaginae were filled with sticky mucus. The uteri were plum coloured, long and wide. Histological comparison of the uteri of the injected and untreated animals showed increased width of the muscular coat and an increased number of glandular tubules in the hyperaemic and oedematous mucosa.

From 5 similar experiments carried out on mice, 3 yielded positive and 2 negative results.

Summary.

In 9 out of 13 experiments the injection of heterologous semen had caused a marked effect on the female genitalia. From this we drew the conclusion that semen probably contains an active principle apart from its fertilizing potency which under favourable circumstances has a stimulating effect upon the female genitalia. To these preliminary investigations one of us referred in his paper (Green-Armytage, 1943), stressing the fact that further experiments were necessary to elucidate the process or processes involved. The aim of these experiments was to gather facts with a view to

(*a*) Defining as clearly as possible the stimulating action of semen on the ovaries and uteri, and the conditions in which such an effect can be obtained.

(*b*) Establishing whether, and if so to what extent, the effect upon the uterus is dependent upon the ovaries.

(*c*) Determining the causes of the discrepancies observed in our preliminary experiments, that is to find out why in a comparatively high percentage of the experiments the female genitalia were not influenced by the injections.

(*d*) Investigating whether, and if so how, hypophysectomized animals react to semen injections.

The difficulties of obtaining the necessary animals together with war-time and post-war conditions caused a regrettable delay. In this paper we are giving a report upon experiments concerned with the problems summarized under (*a*) and (*b*).

I. *Human semen injected into immature animals.*

This series comprises 22 experiments on immature rats and rabbits. The injected

TABLE I

No.	Species and Size of Litter	Treatment	Results: Ovaries — Macroscop. Appearance	Ovaries — Histolog. Findings	Uteri — Macroscop. Appearance	Uteri — Histological Findings	Vagina	Remarks
1	2 rabbits 1 inj. 1 control	1 ml. HS i.v. d.×6	Cy+ S+	FoM++ Lut+++	S+ Hyp++ LMuF D+	Hyp+++ gl. tub+++ Ed+ Musc.++ cub++v		
2	3 rabbits 2 inj. 1 control	1 ml. HS i.v. d.×10	Cy+ S±	FoM+R	S+ Hyp+ LMuF D+	Hyp+ gl. tub+++ Ed+ Musc.+++		
3	5 mice 3 inj. 2 controls	0.2 ml. HS×2 i.m. d.×5	S+	FoM+++ Lut+	S+ Hyp+ D++	Hyp++ gl. tub.+++ Ed+	open 3rd day dioestrus contr. clsd. throughout	
4	2 rabbits 1 inj. 1 control	1 ml. HS i.v. d.×8	S+	FoM+R	L+	gl. tub.+ Musc.+		
5	3 rabbits 2 inj. (1) (2) 1 control (3)	1 ml. HS. i.v. a.d.×6	(1) S± C+ (2) S—	(1) FoM+R (2) FoM+R	(1) L+ (2) L++	Musc+ as control		
6	3 rabbits 2 inj. 1 control	2 ml. HS i.v. d×6	Cy+ S+	FoM+++ Lut+++	S+ Hxp++ LMuF D++	Hyp+ gl. tub.+++ Ed+ Musc.++ cub++v		
7	6 rats 4 inj. 2 controls	0.3 ml. HS i.m. d.×5	S+	FoM+++	S+ Hyp+	Hyp+ gl. tub++ Musc.++	open (1) 36 hrs. (2, 3) 48 hrs. (4) 60 hrs. Dioestrus throughout con. cld. throughout	
8	3 rabbits 2 inj. (1) (2) 1 control (3)	1 ml. HS i.v. d.×6	(1) S— Cy+ (2) S±	(1) FoM+R (2) FoM+R	L++ L+	as control as control		
9	2 rabbits 1 inj. 1 control	1 ml.— 2 ml.—HS i.v. 3 ml.— successive days	S+	FoM+++ Lut+	S+ Hyp+ LMuF D++	Hyp+ gl. tub+++ Ed+ HR		Fig. 1, 2

TABLE I (*Continued*)

No.	Species and Size of Litter	Treatment	Results: Ovaries — Macroscop. Appearance	Ovaries — Histolog. Findings	Uteri — Macroscop. Appearance	Uteri — Histological Findings	Vagina	Remarks
10	3 rabbits 2 inj. (1) (2) 1 control (3)	1 ml. HS i.v. d.×8	(1) S— Cy+ (2) S—	FoM+R FoR	L+ L+	gl. tub+ Musc.± Musc+		
11	3 rabbits 2 inj. (1) (2) 1 control (3)	0.6 ml. HS i.v. d.×8	(1) S± Cy+ (2) S—	FoM+R FoR	L+ L++	as control Musc+		
12	3 rabbits 2 inj. 1 control	2 ml. HS i.v. a.d.×4	S+	FoM+++	S++ Hyp+ LMuF D+	Hyp++ gl. tub+++ Ed+ H col.		
13	2 rabbits 1 inj. 1 control	1 ml. HS i.v. a.d.×8	S+	FoM+++ Lut+	S++ Hyp+ LMuF D++	Hyp++ gl. tub.+++ Ed+ H col.		
14	2 rabbits 1 inj. 1 control	1 ml. HS i.v. a.d.×6	S±	as control	L+	Musc.+		

KEY TO TABLES.

inj. injected.
contr. control (not injected).
i.v. intravenously.
i.m. intramuscularly.
s.c. subcutaneously.
d. daily.
a.d. alternate days.
HS. human semen.
HoS. homologous semen.
S. size (length and width) compared with control.
S−. smaller than control.
S± equal to control.
S + (++, +++) bigger (increasing) than control.
L. length.
L± equal to control.
L + (++, +++) longer (increasing than control.
D+ diameter increased, compared with control.
Cy+ cystic.
FoM. follicle stimulation.
FoR retardation of follicle development.
FoM + R. few mature follicles present but majority of follicles less developed than controls.
Lut. luteinization.
Hyp. hyperaemia.
LMuF. lumen dilated and filled with mucus.
Es. oedema.
H. col. high columnar epithelium.
cub. cuboidal epithelium.
v. vacuoles in epithelial cells.
gl. tub. +(++, +++) increased number of glandular tubules present.
Musc.+ thickness of muscular coat (compared with controls).
HR. haemorrhage.
RO. right ovary.
LO. left ovary.
BOE. both ovaries removed.
ROE. right ovary removed.
LOE. left ovary removed.
RH. right uterine horn.
LH. left uterine horn.
RhE. right uterine horn removed.
LHE. left uterine horn removed.
NAD. no abnormality detected.
BA. beginning atrophy.

material was human semen as collected in Sterility Clinics and Laboratories regardless of whether the specimens were produced by healthy donors or otherwise. Eight experiments were negative, that means to say in these 8 assays no difference was found between the ovaries and uteri of the injected animals and those of their litter mates kept untreated as controls.

As will be seen from Table I, in 5 experiments on rabbits, in 1 on rats and in 1 on mice, the autopsy—performed 24 hours after the last injection—revealed an increase in the size of the ovaries, and on histological examination numerous ripe as well as maturing Graäfian follicles were found. In 5 instances a more or less extensive luteinization was noticed. The uteri of the injected does had increased considerably in length and width. They appeared dark red. Their lumen was distended and blocked by congealed mucus. Microscopical examination revealed hyperaemic and oedematous mucous membranes piled up in folds with numerous glandular tubules in each visual field, a stroma rich in cells and a lining epithelium which was either columnar or consisting of two or three layers of cuboidal cells. These epithelial cells as well as those of the glandular tubules often contained vacuoles. Figs. 1 and 2 show the result of such an experiment which was of special interest because of a haemorrhage into the uterine mucosa causing a partial shedding off of the lining epithelium.

Quite different from these findings were the results in other experiments of this series. In these the ovaries of the injected does were either smaller than or of about the same size as the ovaries of the controls. Often small cysts containing a light pink-tinted fluid were observed on their surface. The uteri were usually much longer than their controls but they appeared white, narrow and thread-like. Histological examination of the ovaries showed the presence of few (mostly 2 or 3) large ripe, or almost ripe, Graäfian follicles contrasting with the rest of the follicles which appeared smaller, being at an earlier state of development than the partly-matured follicles in the controls. Microscopical slides of the uterine wall revealed usually little difference between the injected and the control litter mates. Sometimes a moderate increase in the width of the muscular coat was noted but no change in the mucosa.

II. *Human semen injected into spayed mature animals.*

This series consisted of 14 experiments but in only 5 of them striking differences between the injected does and their similarly-spayed litter mates were observed. These successful experiments have been summarized in Table II. It will be seen from this table as well as from Figs. 3, 3c, 4 and 4c, that the atrophic changes in the uterine wall which follow castration were prevented. At autopsy the uteri of the control does were found in varying stages of atrophy, whereas the uteri of the injected animals were hypertrophied and hyperaemic. Histological examination showed that the width of the muscular coat and of the mucosa had increased. The latter was oedematous; its superficial layer rich in intensely stained cells. There were numerous glandular tubules and the epithelial lining consisted of large high columnar cells.

Twice we have repeated these experiments using litters of mature as well as of immature rabbits. (1) Of 12 immature does 3 gave results similar to those recorded in Table II, 5 completely failed to respond to the injections, whereas the uterine horns of 4 injected rabbits were found to have increased in length but not in width. These were much longer than those of their respective untreated litter mates, but histo-

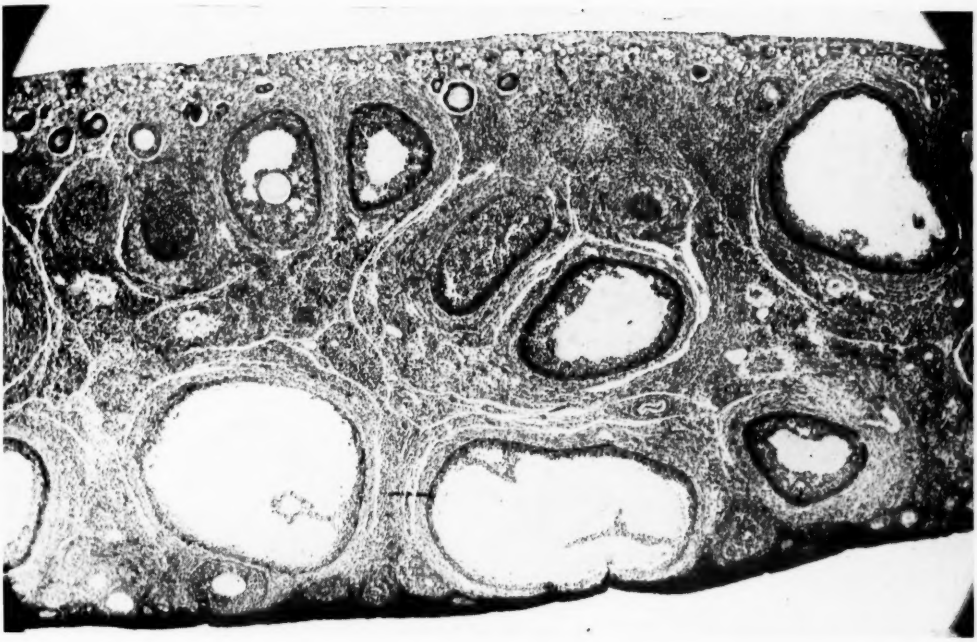


FIG. 1.

Section through an ovary of a 7-weeks-old rabbit after 3 intravenous injections of 1, 2, and 3 ml. respectively of human semen on 3 successive days.
Note numerous mature and almost mature Graafian follicles and a certain degree of luteinization of theca cells.

G. A.

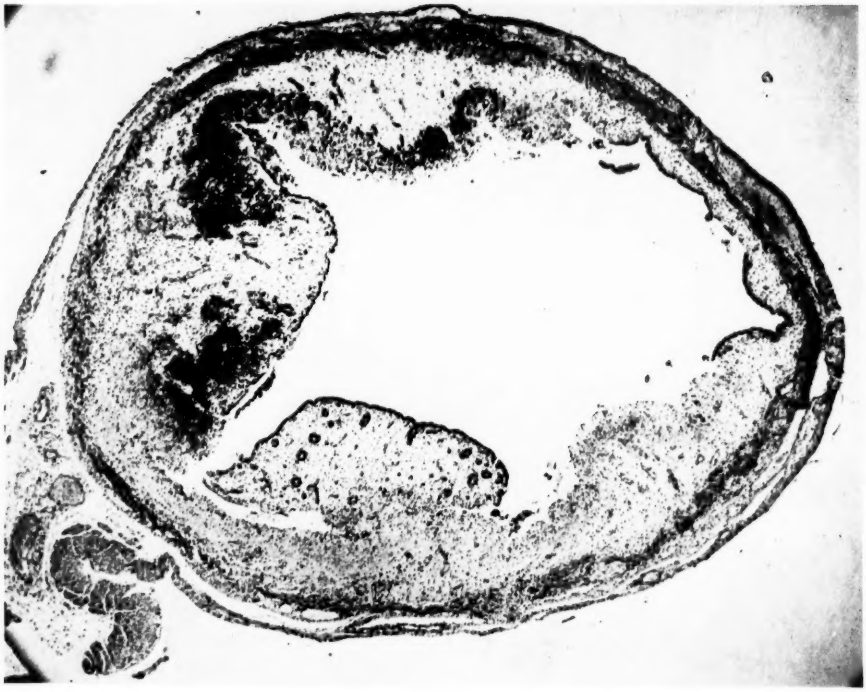


FIG. 2.

Section through the uterine horn of the same rabbit (see Fig. 1). Note hyperaemia and oedema of the mucosa, the increase in the number of glandular tubules and the haemorrhages into the mucosa, the epithelial layer of which is partly shed.

G. A.

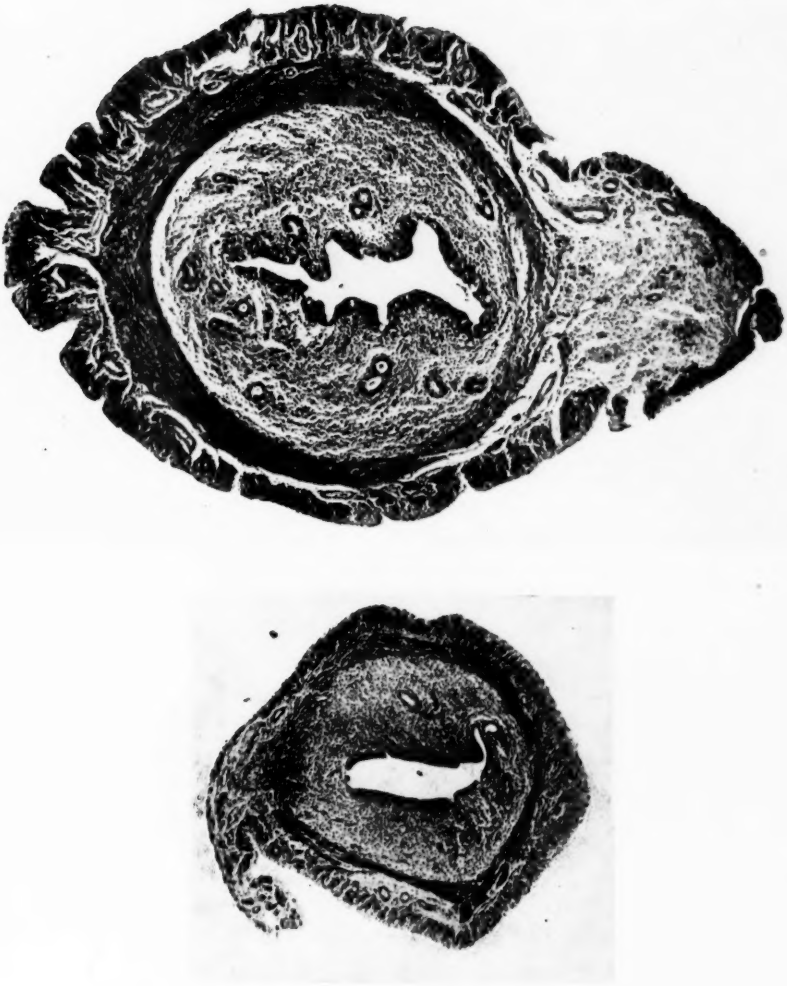
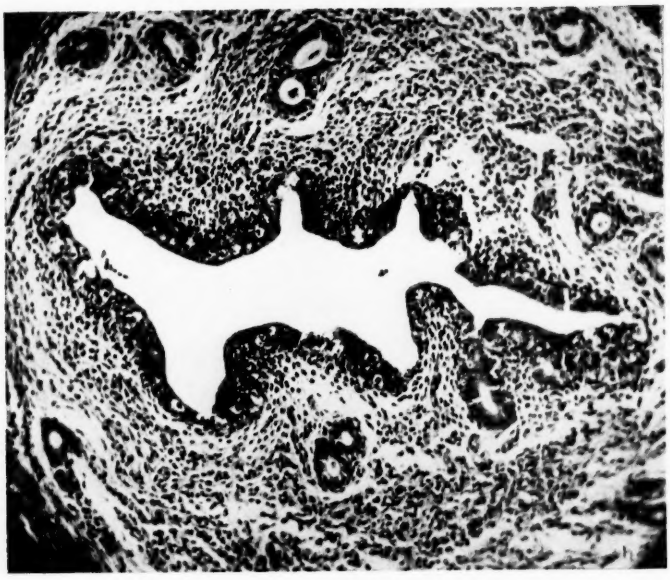


FIG. 3 and 3C.

Sections of the uteri of 2 litter-mate does spayed 24 hours before the experiment was started. "3" received 8 intravenous injections of 1 ml. human semen on alternate days. "3C" is the untreated control.
Note difference in the thickness of muscular coats and mucous membranes between "3" and "3C".

G. A.



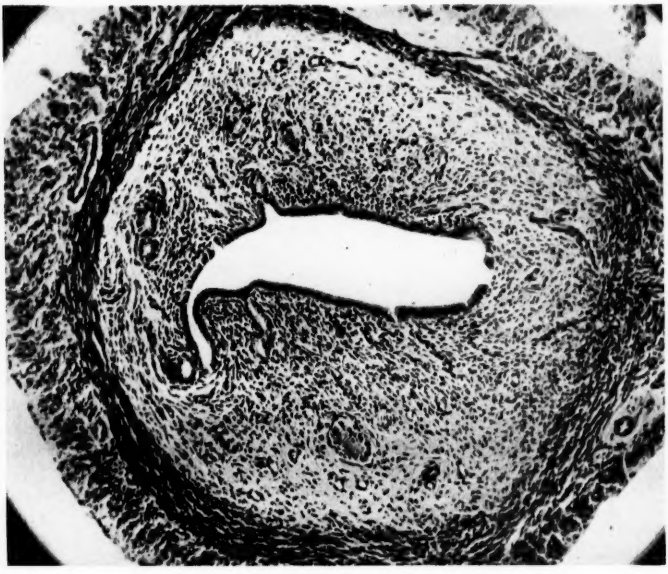
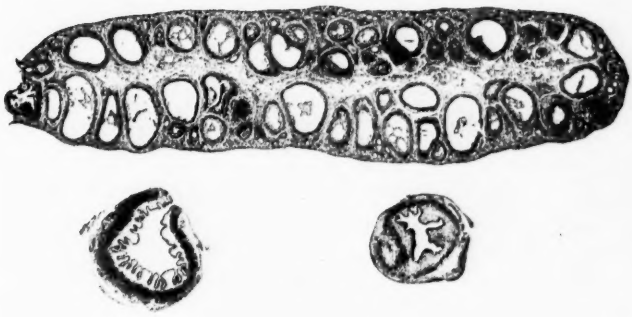


FIG. 4 and 4c.

High magnification of "3" and "3c".

Note the number of glandular tubules in the oedematous mucosa in "4". The epithelial lining consists of 2 or 3 layers of large cells, many of which contain vacuoles.

G. A.



5a.

5b

FIG. 5, 5a, and 5b.

Sections through the ovary and uterine horn of a 7-weeks-old rabbit after 3 intravenous injections of 0.8 ml. of homologous semen given on successive days.
Note follicle stimulation and increased thickness of the uterine wall.

G. A.

FIG. 6.

Uteri of 2 litter-mate does, 3 months old, spayed 1 week before the experiment started. "C" is the uterus of the untreated control. The uterus pictured on the left was removed 24 hours after the last of 3 intravenous injections of 1 ml. homologous semen given on alternate days. Note difference in the size of the 2 uteri.

G. A.

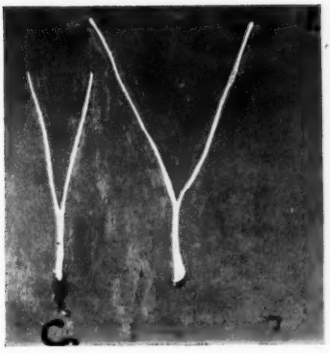


FIG. 7.

Uteri of 2 litter-mate does, 3 months old, spayed 3 weeks prior to the experiment. "C" is the uterus of the untreated control. The experimental animal received 8 intravenous injections of 0.8 ml. of homologous semen.

Note increase in length but not in thickness.

G. A.

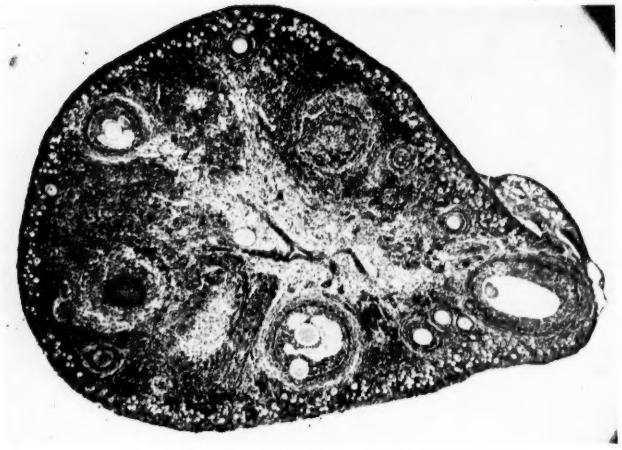


FIG. 8.

Section through left ovary of an 8-weeks-old rabbit removed 24 hours before the first of 7 intravenous injections of 0.8 ml. of homologous semen given on alternate days.

FIG. 9.

Section through the right ovary of the same rabbit (Fig. 8) removed 24 hours after the last injection.

Note in Fig. 8 a fair number of maturing follicles in an approximately equal state of development.

Note in Fig. 9 two mature follicles but absence of further maturation in the other follicles as compared with Fig. 8.

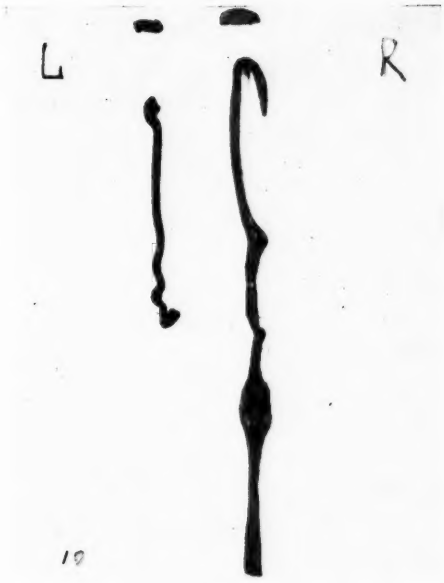


FIG. 10.

L = left ovary and uterine horn of a 2-months-old doe removed 24 hours prior to the start of the experiment.
R = right ovary and uterine horn of the same rabbit removed 36 hours after the last of 4 intravenous injections of 1.0 ml. of homologous semen given on alternate days.
Note increase in size of the right ovary and uterine horn.

G. A.

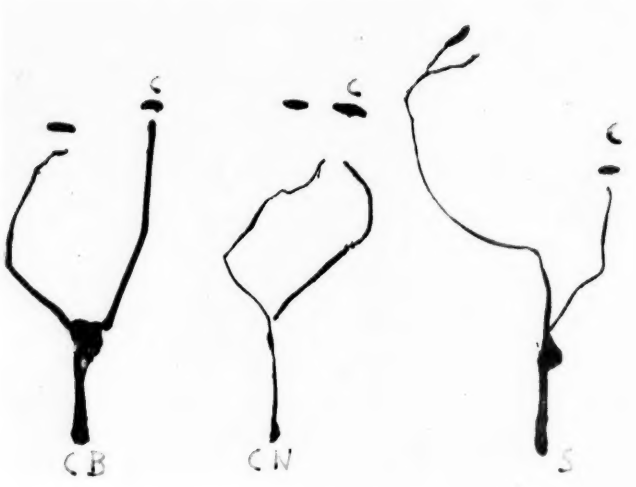


FIG. 11.

Ovaries and uteri of 3 litter-mate does, the right ovaries and uterine horns of which had been removed 24 hours prior to the start of the experiment (marked C). One doe (marked S) received 6 intravenous injections of 0.8 ml. of homologous semen given on successive days. The second doe (marked CB) received 6 intravenous injections of 0.8 ml. of the same semen after it had been heated in a boiling water bath.

The third doe (marked CN) received 6 intravenous injections of 0.8 ml. of normal saline.

The left ovaries and the corpora uteri with the remaining uterine horns were removed 24 hours after the last injection.

NOTE: In CN right ovary slightly larger than left. In CB ovaries of equal size, but right horn is larger than left. In S left ovary is larger and left uterine horn is much longer than right but there is no increase in thickness. Increase in size of the corpora uteri and vaginae of CB and S.

G. A.

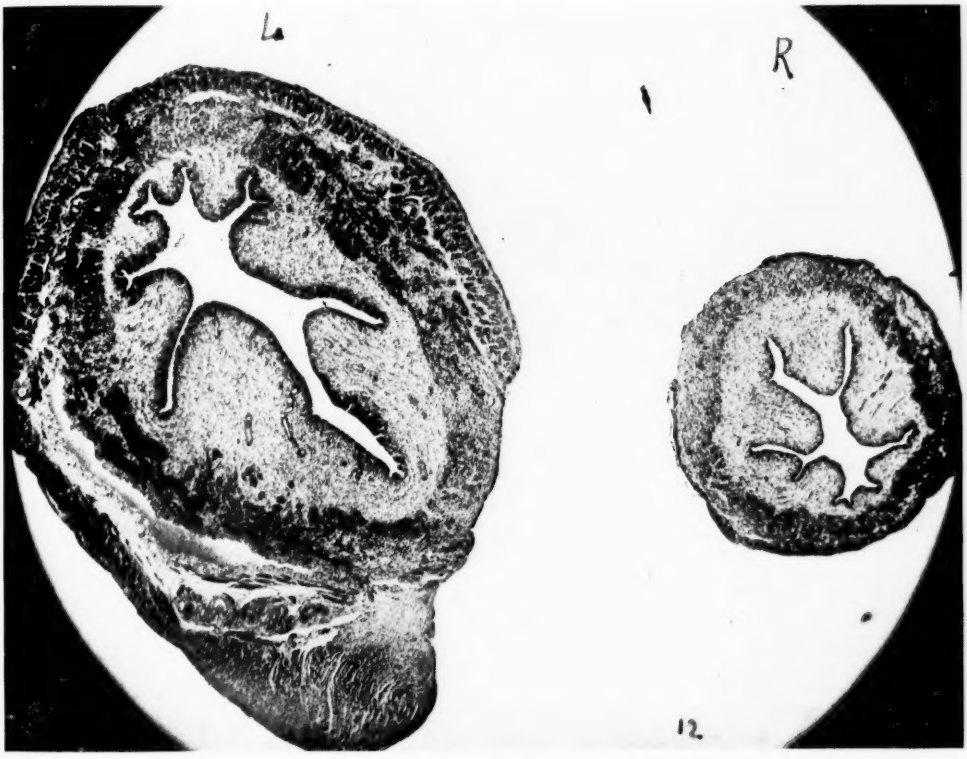


FIG. 12.

Sections through the right (R) and the left (L) uterine horn of an 8-months-old rabbit spayed 4 weeks prior to the start of the experiment.
R was removed 24 hours before the first injection. L was removed 24 hours after the last of 7 intravenous injections of 1 ml. of homologous semen given on alternate days.
Note the difference in diameters between L and R caused by a marked increase in the thickness of the muscular coat and the mucosa in L. Note also the engorged blood vessels, the increase of glandular tubules and the cellular infiltration of the mucosa in L.

G. A.

FIG. 13.

Uterine horns of a 4-months-old doe, spayed 1 week prior to the start of the experiment. The right uterine horn (R) was removed 24 hours before the first of 8 intravenous injections of 0.9 ml. of homologous semen given on successive days. The left uterine horn (L) was removed 24 hours after the last injection.
Note increase in length and width of the (L) horn.

G. A.

TABLE II.—SPAYED MATURE ANIMALS

No.	Species and Size of Litter	Treatment	RESULTS: Uteri — Macroscop. Appearance	Uteri — Histological Findings	Vagina	Fig.
1	3 rabbits 2 inj. 1 contr.	8 days after BOE 1 ml. HS i.v. d. × 6	S+ Hyp+ LMuF. D++	Hyp++ gl. tub++ Hcol.		
2	2 rabbits 1 inj. 1 contr.	8 days after BOE 2 ml. HS i.v. a.d. × 3	S+ Hyp+ LMuF D+	Hyp+++ gl. tub+ Hcol. Musc+		
3	7 mice 5 inj. 2 contr.	6 days after BOE 0.2 ml. HS s.c. d × 10	S+ Hyp+ D+	Hyp+ gl. tub+	At the start : dry After 3rd injection : moist, containing a stringy mucous No oestrus smears obtained	
4	3 rabbits 2 inj. 1 contr.	24 hours after BOE 1 ml. HS i.v. a.d. × 8	S+ Hyp++ LMuF D++	Hyp+ Ed+ gl. tub+++ Hcol. V. Musc+++		3,3C 4,4C
5	3 rabbits 2 inj. 1 contr.	2 weeks after BOE 1 ml.HS i.v. a.d. × 8	S+ Hyp++ LMuF D++	Hyp++ Ed+ gl. tub++ Hcol. Musc+++		

logical examination showed no difference between the uterine walls of treated and untreated animals. (2) Out of 15 litters of fully-grown spayed rabbits 4 responded with uterine growth and hypertrophy of the mucosa, 6 showed only an increase in length of the uterine horns, and the remaining 5 did not differ from their respective controls.

III. *Preliminary experiments upon the nature of the action of semen injection.*

The microscopical appearance of, and in particular the histological findings in, some of the uteri of the does which had been subjected to semen injections were suggestive of progestational changes. In order to establish whether the injected sperm itself possessed any progestational activity, we assayed the effect of semen injections on spayed rabbits primed with stilboestrol. No difference was noticed between the does which had received stilboestrol only and those which after the stilboestrol treatment had been injected with human semen. The results of these experiments were uniform although we used varying amounts of stilboestrol for the priming treatment and more recently substituted boar's sperm or freshly-collected rabbit's sperm for the human semen in the test-injections.

We have performed a few experiments in order to establish whether the action of semen is affected by heat. We pooled the semen of several donors and kept half the quantity in a boiling water bath for 15 minutes. The heated and the untreated semen were injected into different does of the same litter. Whereas a positive result was obtained with the unaltered specimen, the heated portion proved to be inactive.

In view of the fact that heating causes an insoluble protein precipitate to be formed in the seminal fluid the result of these experiments allows of two explana-

tions, viz. either the active principle itself is thermolabile or it is absorbed and engulfed by proteins which are being rendered insoluble by heating.

Finally we investigated the effect of acetone on the semen. We poured pooled semen into 5 times its volume of acetone, and immediately thereafter we separated the acetone soluble fraction from the precipitate. The acetone was evaporated *in vacuo* (at about 37°C). The acetone soluble residue was emulsified in saline whereas the acetone precipitate was thoroughly ground and suspended in acidified saline (pH5). In no instance have we seen the acetone soluble portion to have any action upon the genitalia; whereas the acetone precipitate was potent when obtained from active semen. It would appear, therefore, that the active principle in semen is precipitated by acetone together with its protein-fraction. Whether it is itself a protein or a protein derivative or an acetone insoluble lipid must be determined by further experiment.

In view of the fact that the volume of one human ejaculate is comparatively small and that pooling of different samples of unknown activity might confuse the issue, we decided to use animal semen, and in particular boar's semen, which is voided in quantities of several hundred ml. at a time.

We are greatly obliged to Dr. A. Walton of the Animal Research Station, Cambridge, for kindly supplying us with boar's sperm in 1944. We divided the large amount of one ejaculate into smaller portions and kept them in a frozen state. Prior to any single experiment the material needed was thawed and the rest left untouched. One hundred ml. of boar's sperm were slowly poured during constant stirring into 400 ml. of acetone. The precipitate was quickly separated from the supernatant fluid, dried *in vacuo* at low temperature and then extracted with 200 ml. of benzene. After 24 hours the benzene was replaced by another 200 ml. of fresh benzene. Twenty-four hours later the 2 batches of extract were pooled, filtered and made up again to 400 ml. with benzene. Of this, 100 ml. were evaporated and the residue dissolved in 10 ml. of pure olive oil. Two immature rabbits of a litter of 3 received intramuscular injections of 2 ml. of this oily solution on 2 subsequent days. Forty-eight hours after the second injection the 3 litter mates were killed. At autopsy the ovaries of the injected does were found to be much larger than were those of the control rabbit. Striking was the difference in the appearance of the uteri. The control was pale and thread-like, whereas the uteri of the injected animals appeared dark red, large and coiled. Their lumen was distended and filled with a stiff mucus. Histological examination revealed the presence of numerous mature as well as ripening follicles in the ovaries. The uterine vessels were engorged, the diameter of the uterine mucosa was about twice that of the control. Glandular tubules were abundant but there was no sign of secretion. The endometrial lining consisted of large darkly-stained cuboidal cells without vacuoles.

Another 200 ml. of the benzene extract were poured with constant stirring into 800 ml. of acetone. The resulting white precipitate was collected on a dense filter and redissolved in 20 ml. benzene. The clear benzene solution was put on an electric water bath and, when almost evaporated, 10 ml. saline were added. This emulsion was tested on 2 immature does. The result was identical with that just described as a sequelae of the injection of the unprecipitated benzene extract.

These experiments suggest that the effect of semen injection is entirely, or at least partly, due to one or more factors which are insoluble in acetone but soluble in benzene.

Insemination.

Although insemination would appear to be the ideal method of reproducing physiological conditions, it must be realized that such a means is fraught with many difficulties and fallacies. For instance, manipulation of the rodent vagina may produce ovulation (rabbit, ferret) or pseudo-cyesis or both. For this reason we used only spayed rabbits and guinea-pigs for our insemination experiments. After prolonged and intensive treatment we have observed hyperaemia and increase in size of the uteri, glandular proliferation and cell infiltration in the uterine mucosa; the epithelial lining of the mucosa consisting in 2 or 3 layers of large cuboidal cells, many of which contained vacuoles. But in spite of this we are reluctant to draw any conclusions from these experiments as similar results were obtained with boiled semen, which, when injected intravenously, had proved to be inactive. It remains to be seen whether the inactivation of semen by heat is a reversible process. If so, the results of insemination with heated sperm would not only be explained but would even *a fortiori* prove the effectiveness of semen absorption through a mucous membrane. In order to clear this problem we intend to continue insemination experiments on hypophysectomized rabbits and it is to be hoped that fresh experiments will be undertaken on these lines in South Africa where baboons are readily procurable and the results can be checked and followed up.

Homologous Semen.

Although experimentation with fresh boar's sperm is a protection against certain fallacies connected with the use of semen from sterility clinics we realized that the necessity of keeping the material frozen for several days or even weeks involved the risk of deterioration of the substance. We came, therefore, to the conclusion that it was preferable to use fresh rabbit sperm from our own animals which was obtainable at any time desired in the course of our experiments. Moreover, since for obvious reasons it is preferable to avoid the introduction of foreign protein, we confined ourselves to experiments with rabbits.

The first series of experiments with rabbit semen was carried out on 12 litters of does using the same technique as we used in our experiments with human sperm. In 8 of these 12 assays the injection of homologous sperm had a definite influence on the reproductive apparatus of the rabbits (see Table III). Figs. 5, 5a and 5b illustrate the effect on an ovary and a uterine horn of a 7-weeks-old doe. Follicle-stimulation and precocious development of the uterus were brought about by 3 intravenous injections of 0.8 ml. of freshly collected rabbit sperm. In Fig. 6 we see that the semen injections have not only warded off the effect of spaying on the uterus, but have produced marked hypertrophy. In contrast to such findings are the results of other experiments of which Fig 7 shows a typical example. There we see that the injections have caused the uterine horn to grow longer but there was no difference in the width of the horns of the control animal on one side and of the injected doe on the other.

Admittedly it is extremely difficult to assess results in border-line cases by roughly measuring the uterine horns of 2 different rabbits even though they are litter mates; but these border-line cases are of great interest and importance from the human clinical standpoint, in that the growth of the immature uterine horns is analogous to the development seen to occur in the hypoplastic uteri of women after weeks or months of marriage. In order to eliminate as far as possible this source of error and obtain an objective yardstick for the assessment of results, we devised the

TABLE III

No.	Age and Size of Litter	Treatment: Prior to Semen Inject. Time	Treatment: Actual Experiment	RESULTS: Ovaries: Macrosc. Appear.	RESULTS: Ovaries: Histolog. Findings	RESULTS: UTERI: Macroscop. Appearance	RESULTS: UTERI: Histolog. Findings	Fig.
1	3 rabbits	48 hours BOE	(1) 0.5 ml. HoS i.v. a.d.×8 (2)			S++ Hyp++ LMuF	Hyp++ Ed++ Hcol. gl. tub.+Musc.+	
	5 months		(3) 0.5 ml. saline i.v. a.d.×8 contr.			Thin, pale	BA	
2	2 rabbits		(1) 0.8 ml. HoS i.v. d.×3	S+	FoM Lut+	S++ Hyp+ LMuF	Hyp+ Musc.++ Hcol c++	5, 5A, 5B
	7 weeks		(2) 0.8 ml. saline i.v. d.×3 contr.		immature	thin, pale	NAD	
3	2 rabbits	3 weeks BOE	(1) 0.7ml. HoS i.v. a.d.×8			L++ thin, pale	not examined	7
	3 months		(2) 0.7 ml. saline i.v. a.d.×8 contr.			pale	not examined	
4	2 rabbits	1 week BOE	(1) 1 ml. HoS i.v. a.d.×3			S++ Hyp+++	not examined	6
	4 months		(2) 1 ml. saline i.v. a.d.×3 contr.			pink	not examined	
5	2 rabbits		(1) 0.5 ml. HoS i.v. d.×8	S+	FoM+R Lut 0	S+ Hyp+ LMuF	Hyp+ gl. tub++ Hcol.+Musc.+	
	7 weeks		(2) 0.5 ml. saline i.v. d.×8 contr.		immature	thin pale	not examined	
6	3 rabbits		(1) 0.8ml. HoS i.v. d.×8 (2)	S±	FoM+ Lut 0	L+ thin, pale	NAD	
	9 weeks		(3) 0.8 ml. saline i.v. c.×8 contr.		immature	thin, pale	not examined	
7	2 rabbits		(1) 0.7 ml. HoS i.v. d.×8	S±	FoM+R Lut 0	L+ thin, pale	Musc.+	
	8 weeks		(2) 0.7 ml. saline i.v. c.×8		immature	thin, pale	NAD	
8	2 rabbits		(1) 0.7 ml. HoS i.v. d.×6	S±	as control	L++thin pale	as control	
	9 weeks		(2) 0.7 ml. saline i.v. c.×6 contr.		NAD	thin, pale	NAD	

following technique for further experiments. When unspayed animals were used, we removed the ovary and the whole uterine horn of one side 24 hours before starting with the actual assay, making sure at the time of laparotomy that the other ovary and horn were not longer or larger than the amputated organs. The latter were preserved in Bouin's solution. Twenty-four to thirty-six hours after the last injection the does were killed and at the necropsy the corporate ovary and uterine horn were carefully dissected out and also placed in Bouin's fluid. A few days later, when well fixed, the two ovaries and horns were compared.

Bearing in mind that during the days of experimentation a certain amount of growth is physiological, we used a litter mate as a control, subjecting it to the same operation but not to any seminal fluid injection. This enabled us to estimate how much the increase in the size of the organs of the experimental animals was physiological and how much due to the injections.

Twelve experiments on unspayed litters were carried out with this technique (see Table IV). In 3 there were no definite differences between the ovary and the uterus removed before and after the injection. Six of the remaining 9 litters were immature. The ovarian response to injections of homologous semen in these animals was either generalized follicular stimulation or maturation of a very few follicles with simultaneous retardation of the remainder as will be seen in Figs. 8 and 9, which picture the ovary of an 8-weeks-old rabbit which was subjected to such an experiment. Such stimulation and retardation of the follicles is an interesting feature deserving further investigation. Noble (1939) made a similar observation in immature rats after prolonged treatment with testosterone proportionate injections and we also made note of this result in our earlier experiments with human semen (*vide* page 328).

The above technique proved especially helpful in assessing the effects upon the uteri. All the horns removed at the end of the experiments had considerably increased in length as compared with the corresponding horns amputated before the first injection (*vide* Fig. 10). In some experiments we found that the horns had also increased in width and in these histological changes were observed similar to those described above.

Fig. 11 is a photograph of the uterine horns and ovaries of 3 litter-mate does. "S" was injected with untreated sperm; "CB" with boiled sperm and "CN" with normal saline.

The ovaries of "S" differ in size, the left one being larger than the control; the comparison of the two horns is interesting, for whereas there is no difference in their width, both being thread-like, the left horn had grown to more than double the length of the right.

The injection of boiled semen (CB) had no effect on the size of the ovary but it is noteworthy that the right uterine horn which was amputated prior to the injections was found to be larger than the left one. Moreover, the amputated ovary of the control doe (CN) was larger than the corresponding organ observed at autopsy. Besides, it will be seen that the corpora uteri and vaginae of the does "CB" and "S" are much thicker than the corpus of the control doe "CN". We have noted these facts without being able to offer an explanation.

Finally, we have to report the results of 16 experiments on spayed litters using this technique. Five of these were negative. The most interesting conclusion, which we have drawn from the remaining 11 assays, is that semen injections were able to prevent those atrophic changes that take place after

TABLE IV.—UNSPAYED ANIMALS

No.	Age and Size of Litter	Treatment: Prior to Semen Inj. Time	Treatment: Actual Experiments	Results: Ovaries: Macroscop. Appearance	Results: Ovaries: Histolog. Findings	Results: Uterus: Macroscop. Appearance	Results: Uterus: Histolog. Findings	Fig.
1	2 rabbits	24 hrs. : LOE+LHE	(1) 0.8 ml. HoS i.v. d.×7	RO=LO	RO : FoM+R	RH : S++ Hyp+	RH : Hyp++ Hcol+ gl. tub++ Musc++	8+ 9
	8 weeks		(2) 0.8 ml saline i.v. d.×7 contr.	small	immature ovary	white, thin RH=LH	NAD	
2	4 rabbits	24 hrs. LOE+LHE	(1)	RO LO	FoM±	RH : LH=65 : 39 S+	Hyp+ Hcol.	
			(2) 0.8 ml. HoS i.v. d.×5	RO=LO	FoM+R	RH : LH=58 : 32 S+	gl. tub+	
	9 weeks		(3)	RO LO	FoM+R	RH : LH=62 : 33 S+	Musc++	
			(4) 0.8 ml. saline i.v. d×5 contr.	RO=LO	RO=LO	thin, small R : L=41 : 37	RH=LH	
3	2 rabbits	24 hrs. ROE+RHE	(1) 1 ml. HoS i.v. a.d.×8	LO : Cy	LO : Hyp++	LH : RH=130 : 95	NAD Hyp+	
	1 year		(2) 1 ml. saline i.v. a.d.×8 contr.	RO=LO	RO=LO	LH : RH	NAD	
4	2 rabbits	24 hrs. LOE+LHE	(1) 0.8 ml. HoS i.v. a.d.×5	RO=LO	RO : Hyp+ FoM+R	RH : LH=85 : 55 L+	NAD	
	2 months		(2) 1 ml. saline i.v. a.d. × 5 contr.	RO=LO	RO=LO	RH : LH=60 : 52	NAD	
5	2 rabbits	24 hrs. LOE+LHE	(1) 1 ml. HoS i.v. a.d.×4	RO : S+	Not examined	RH : Hyp+ L+	Not examined	10
	2 months		(2) 1 ml. saline i.v. a.d.×4 contr.	RO=LO	not examined		not examined	

TABLE IV. (*Continued*)

No.	Age and Size of Litter	Treatment: Prior to Semen Inj. Time	Treatment: Actual Experiments	Results: Ovaries: Macroscop. Appearance	Results: Ovaries: Histolog. Findings	Results: Uterus: Macroscop. Appearance	Results: Uterus: Histolog. Findings	Fig.
6	3 rabbits	24 hrs. LOE+LHE	(1) 0.8 ml. HoS i.v. d.×6	LO larger RO	not examined	LH longer but not larger than RH	not examined	
	2 months		(2) 0.8 ml htd. HoS i.v. d.×6	RO=LO	not examined	RH thicker than LH	not examined	11
			(3) 0.8 ml. saline i.v. d.×6 contr.	RO larger LO	not examined	LH=RH	not examined	
7	2 rabbits	24 hrs. ROE+RHE	(1) 1 ml. HoS i.v. d.×10	LO : Cy+	LO=RO	LH : RH=105 : 80	LH : Hyp+ gl. tub+	
	8 months		(2) 1 ml. saline i.v. d.×10 contr.	LO=RO	LO=RO	LH : RH=87 : 76	LH=RH	
8	2 rabbits	24 hrs. LOE+LHE	(1) 1 ml. HoS i.v. a.d.×8	RO=LO	RO=LO	RH : L+ RH : LH=75 : 58	RH=LH	
	10 mths.		(2) 1 ml. saline i.v. a.d.×8 contr.	RO=LO	RO=LO	RH : LH=69 : 63	RH=LH	
9	2 rabbits	24 hrs. ROE+RHE	(1) 0.8 ml. HoS i.v. d.×7	LO : S+	FoM+ Lut+	LH : S+ RH : LH=35 : 60	LH : Hcol+ Musc++ gl. tub+	
	2 months		(2) 0.8 ml. saline i.v. d.×7 contr.	LO=RO	LO=RO	RH : LH=37 : 48	RH=LH	

TABLE V.—SPAYED ANIMALS

No.	Age and Size of Litter	Treatment: Prior to Semen Inj. Time	Treatment: Actual Experiments	Uterus: Macroscopical Appearance	Uterus: Histological Findings	Fig.
1	2 rabbits	24 hrs. : BOE+LHE	(1) 0.7 ml. HoS i.v. a.d.×10	RH : LH=84 : 69 L+ thin pale	NAD	
	10 mths.		(2) 0.7 ml. saline i.v. a.d.×10 contr.	RH : LH=48 : 61	BA in RH	
2	3 rabbits	2 weeks BOE	(1) 0.8 ml. HoS i.v. d.×8	LH : RH=67 : 48 S++ Hyp+	LH : Hyp++ Hcol gl. tub+	
			(2) 0.8 ml. HoS i.v. d.×8	LH : RH=70 : 59 S+	LH : Hyp+	
	6 months	24 hrs. RHE	(3) 0.8 ml. saline i.v. d.×8 contr.	LH : RH=42 : 54 thread like	BA	
3	2 rabbits	4 weeks BOE	(1) 1 ml. HoS i.v. a.d.×7	LH : S+++ Hyp+++ D+++ S+ LMuF	LH : Hyp++ cub+++V gl. tub++ Musc++	12
	8 months	24 hrs. RHE	(2) 1 ml. saline i.v. a.d.×7 contr.	LH=RH thin, white S—	LH=RH atrophic	
4	2 rabbits	4 weeks BOE	(1) 0.6 ml. HoS i.v. a.d.×8	LH : S+ Hyp++ LMuF LH : RH=58 :29	LH : Hyp+ cub. gl. tub++ Musc++	
	8 months	24 hrs. RHE	(2) 0.6 ml. saline i.v. a.d.×8 contr.	thin, pale LH : RH=34 : 30 S—	BA	
5	2 rabbits	24 hrs. BOE+RHE	(1) 0.8 ml. HoS i.v. a.d.×8	LH : S++ Hyp+ D+++ LMuF	LH : Hyp+ Ed+++ gl. tub++ Musc++	
	3 months		(2) 0.8 ml. saline i.v. a.d.×8 contr.	thin, pale	NAD	

TABLE V. (*Continued*)

No.	Age and Size of Litter	Treatment: Prior to Semen Inj. Time	Treatment: Actual Experiments	Uterus: Macroscopical Appearance	Uterus: Histological Findings	Fig.
6	2 rabbits	24 hrs. BOE+LHE	(1) 0.6 ml. HoS i.v. a.d.×9	L+	RH : LH=63 :38	RH : Hyp+ Musc+	
	7 weeks		(2) 0.6 ml. saline i.v. a.d.×9 contr.	pale, thin	RH : LH=32 : 36	RH : BA	
7	2 rabbits	24 hrs. BOE+RHE	(1) 0.7 ml. HoS i.v. d.×7	LH : L+	RH : LH=38 : 59	NAD Musc+	
	10 weeks		(2) 0.7 ml. saline i.v. d.x.7 contr.	L—	RH : LH=33 : 39	NAD	
8	2 rabbits	24 hrs. BOE+RHE	(1) 0.5 ml. HoS i.v. a.d.×8	LH : L++	RH : LH=24 : 52	NAD	
	6 weeks		(2) 0.5 ml. saline i.v. a.d.×8 contr.	LH : thread like L—	RH : LH=26 : 20	LH : BA	
9	2 rabbits	1 week BOE	(1) 0.9 ml. HoS i.v. d.×8	LH : S++ Hyp+		not examined	
	4 months	24 hrs. RHE	(2) 0.9 ml. saline i.v. d.×8 contr.	LH=RH		not examined	13
10	2 rabbits	2 weeks BOE	(1) 0.8 ml. HoS i.v. a.d.×7	RH : L+	RH : LH=53 : 30	RH : H col gl. tub+	
	10 weeks	24 hrs. LHE	(2) 0.8 ml. saline i.v. a.d.×7 contr.	RH : S—	RH : LH=30 : 35	RH : BA	
11	2 rabbits	24 hrs. BOE+LHE	(1) 0.7 ml. HoS i.v. a.d.×8	RH : L+	RH : LH=62 : 39	RH : Musc+	
	7 weeks		(2) 0.7 ml. saline i.v. a.d.×8 contr.	RH : L—	RH : LH=25 : 35	RH : BA	

castration. Moreover, regrowth in the remaining horn of a uterus which had already shown atrophic changes has been observed. Figs. 12 and 13 illustrate this fact. On the other hand it will be seen from Table V that the reaction of the uteri of spayed does to semen injections mostly consisted only in an increase in length.

Discussion.

First it is necessary to focus attention on those experiments which gave positive results:

1. The ovarian response of immature animals to semen injections can be grouped in two ways, namely, those in which the semen injections were followed by follicle stimulation leading to the well-known histological picture of an ovary studded with mature or almost mature follicles. These ovaries were usually much larger than their respective controls. In the second group the ovaries not only failed to increase in size but were even smaller than the controls, the histological section revealing a picture characterized by the presence of a few large follicles side by side with small ones. This obviously suggests a dual effect—viz. stimulation of a few follicles and retardation in the development of others. Noble made a similar observation in immature rats treated with testosterone proportionate injections. It may be tempting to interpret our findings likewise as a testosterone effect. We are, however, reluctant to do so because it is not known how much testosterone or similarly-acting substances are contained in the injected semen. This question must be left in abeyance until more is known about the principle or principles responsible for the effects of semen injections, for it should be borne in mind that semen is a complex fluid consisting of the secretions of the testis, the seminal vesicles and the prostate. It is very probable that such a material contains several active substances which may influence one another either in a synergistic or antagonistic or even in a complementary way.

2. The uterine response of the spayed and unspayed mature and immature animals consisted in an almost uniform increase in length, although the reaction of the mucosa seemed to vary to some extent with the presence or absence of the ovaries. This observation suggests that the semen injections act directly on the myometrium; it appears, however, that the effect on the mucosa depends also upon other factors.

Bachsich, Sharman and Wyburn (1945) found in their otherwise negative experiments with semen from "sterility" clinics a slight uterine hypertrophy in immature guinea-pigs after parenteral seminal injections. They did not regard this as significant. We cannot follow them because to us this effect on an immature uterus is of the greatest importance, in that the basis on which our experiments rest is the clinical finding that the immature uteri of virginal women start to grow under the influence of regular sex life. It may also be recalled that Deanesly and Parkes (1937) found the size of the uteri to have increased after treatment with testosterone. It is suggestive to interpret such maturation as being the effect of some substance in the semen because uterine hypoplasia in young women is commonly associated with non-ovulation or, at least, immaturity of the ova. Moreover, it will be recognized that such women begin then to menstruate regularly, whereas formerly their cycles were indeterminate, suggesting that semen contains a complementary factor to an ovarian amboceptor enabling the uterine mucous membrane to act as a receptor.

Such a hypothesis is not necessarily contradicted by the fact that we often failed to demonstrate any ovarian response in our experiments when uterine growth was

noted, for it must be recalled that the ovaries are under the constant influence of the anterior pituitary which may enhance or inhibit the effect of any exogenous stimulus. It is not without interest to recall that in certain Eastern countries young women start having regular intercourse with their husbands directly after the first menstrual period has occurred (10 to 13 years). It is, however, a thing of great rarity for conception to take place within a year or more of married life, which would suggest that maturation of the ovary and uterus is stimulated and completed by the absorbed semen.

The variety of ovarian and uterine changes following semen injections suggests that the results depend not only on the nature of the injected material but also to a similar extent on the phase of the receptor organ. This may explain why 30 per cent of our experiments were failures even when freshly-collected homologous semen was employed.

The part which the ovary and the pituitary play in uterine development is now well established; the action of the adrenals, however, is not so well defined although there is no doubt that androgens of cortical origin exercise an influence on the female genitalia. It is, therefore, assumed that the effect of semen injections on the uterus will not only depend on the nature and the quantity of the active principles in the introduced material but also on simultaneous hormonal influences from the ovaries, the pituitary and the adrenals.

In order to analyze the mode of action it will, therefore, be necessary

(*a*) To use animals in which the hypophysis, the adrenals or both have been removed.

(*b*) To isolate the active principles and establish the action of such on spayed and unspayed immature animals.

(*c*) It is suggested that similar experiments be carried out on baboons, because the generative cycle in primates is the same as that in homo sapiens, whereas the cycle in lower animals is not comparable to that seen in man.

Summary.

1. Semen injections have a follicle stimulating effect upon the ovaries of immature animals; sometimes such injections have a dual effect, viz. stimulation of a few and retardation of many follicles.

2. Seminal injections cause uterine horns to grow in length and in some instances also glandular hyperplasia and oedema of the uterine mucosa are observed.

3. Positive results were obtained in 53 per cent when human semen from Sterility Clinics was used, while freshly-collected homologous animal sperm yielded 70 per cent of positive results.

4. The results of insemination were inconclusive. Reasons are submitted.

5. Attempts have been made to extract and precipitate the active principle or principles in semen.

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The Rh Factor in Obstetrics

BY

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INTEREST in the Rh factor has greatly increased during the past few years, especially since the establishment of its role in intragroup transfusion reactions and haemolytic disease of the newborn (Levine *et al.*, 1941; Boorman, Dodd and Mollison, 1942; Race *et al.*, 1943). There seems little doubt that Rh incompatibility between mother and foetus plays a decisive role in certain foetal conditions now grouped under the term "haemolytic disease of the newborn." Since the aetiology of a large group of pathological conditions in obstetrics in still unknown, various authors have attempted to relate many of these conditions to Rh and other antigenic incompatibility between mother and foetus. Quigley (1945) and others suggested that a possible connexion exists between blood-incompatibility in husband and wife and habitual abortion. Schwartz and Levine (1943) point to the importance of the Rh factor in cases of late abortion. Its possible relation to toxaemia of pregnancy has also been suggested (Javert, 1942). In an extensive study on the importance of the Rh factor in various obstetric conditions, Harrison and Meacock (1945) have not found evidence to suggest any connexion between the Rh factor and abortion, toxaemia of pregnancy and a number of foetal conditions other than those due to haemolytic disease of the newborn.

During the past 3 years we have studied the relation between the Rh factor and several groups of pathological conditions in obstetrics. The results of these studies will be reported below:—

MATERIAL AND METHODS.

Sterile samples of blood for Rh determination and detection of Rh antibodies were taken from 244 women suffering from various obstetric conditions. The tests were performed as follows: A 2 per cent suspension from the blood clot, after removal of the serum, was prepared in normal saline. A drop of this suspension was added to a drop of Rh test serum and incubated in a water bath at 37°C. for one hour. Results were then read macroscopically and microscopically. The test sera used were those of Rh_0 antiserum* and human Rh_0 antisera obtained from patients. At the beginning of this study only anti Rh_0 sera were available. Later on the determinations were performed with 3 anti Rh sera (Rh_0, Rh', Rh"). In all Rh negative cases, the patients' husbands' typing was also performed, and in part of the cases the Rh factor of the children was studied. The sera of the Rh negative women were tested for Rh antibodies. At first, only the agglutination test was performed; later on, however, the "blocking" as well as

* Obtained from Certified Blood Donor Service, Jamaica, N.Y.

"conglutination" reactions were performed.

The technique employed for the agglutinating, blocking and conglutinating methods were those described by Wiener (1945).

In the evaluation of the role played by the Rh factor in any disease-group, 2 elements were considered: the rate of the Rh negative women among those affected, and the detection of Rh antibodies in them.

In a previous study we have found that the rate of Rh negative women in our community is 9.6 per cent (Gurevitch, Brzezinsky and Polishuk, 1947).

I. *The Role of the Rh Factor in the termination of pregnancy during the first 28 weeks (i.e. abortion).*

(*a*) *Habitual abortion.* For the purpose of this study a diagnosis of habitual abortion was assigned only for cases in which at least 3 consecutive abortions have occurred and in which no previous pregnancy had lasted longer than 28 weeks. Cases in which anatomical or general disorders were found, and could account for the abortions, have been excluded from this study. In all cases syphilis was excluded by the Wassermann and Kahn tests in both husband and wife. We have studied a total of 41 cases of habitual abortion and have found among them only 3 Rh negative women, a rate of 7.3 per cent (Table I).

(*b*) *Other forms of abortion.* This group includes cases of repeated abortions, single abortions and missed abortions. Under the term "repeated abortion" are included women who had 2 abortions, or more than 2 abortions with at least 1 normal delivery. Cases in which a definite cause (anatomical or general) for abortion was found have been excluded. The results of determinations of the Rh factor in these cases are reported below in Table I.

TABLE I

Clinical diagnosis	No. of cases	Rh negative	Percentage	Rh positive	Percentage
Habitual abortion	41	3	7.3	38	92.7
Repeated abortion	22	1	4.5	21	95.5
Single abortion	59	6	10.2	53	89.8
Missed abortion	12	2	16.6	10	83.4
	134	12	8.9	122	91.1

As can be seen from Table I, the incidence of Rh negative women in all the forms of abortion does not exceed that found in the population at random. The number of cases of "missed abortion" is too small to permit any conclusions in this respect. Rh antibodies were not detected in the Rh negative cases. This fact coupled with the low incidence of Rh negative women in this group permits the conclusion that no relation exists between Rh incompatibility and abortion.

A characteristic case of repeated abortion which on clinical grounds alone would be suspected of Rh incompatibility is reported below:

Mrs. A. L., aged 32. Her past obstetric history is as follows: The first pregnancy (1939) terminated with the delivery of a male child at term. Her second pregnancy (1941) ended with a stillbirth at the 8th month. The patient's subsequent 3 pregnancies (1942, 1943, 1945) ended in spontaneous abortions in the 2nd and 3rd months. General and gynaecological examinations revealed no cause for the repeated abortions. Blood chemistry was normal. Blood typing revealed the patient to be ARh_1 and her husband ORh_1. Wassermann and Kahn examinations were negative. No antibodies were found in the patient's blood. In this case the normal delivery followed by an unexplained stillbirth and 3 consecutive abortions gave rise to the suspicion that Rh incompatibility played a role in the aetiology. The haematological findings, however, did not confirm this suspicion.

II. *Foetal Pathology in the last Trimester of Pregnancy.*

This group includes cases of stillbirths, macerated foetuses and premature deliveries in which no apparent cause for the condition could be determined. It is to be stressed that toxaemia of pregnancy, diabetes, syphilis and other general conditions were excluded from this group of cases. In Table II we have reported the Rh distribution in this group.

TABLE II.

Diagnosis	No. of cases	Rh negative	Percentage	Rh positive	Percentage
Stillbirths ...	15	2	13.3	13	86.7
Maceration ...	10	1	10.0	9	90.0
Prematurity ...	23	2	8.6	21	91.4
Total ...	48	5	10.4	43	89.6

Rh antibodies in the maternal blood were not detected in any case examined from 6 to 20 days postpartum. It is, therefore, apparent that the stillbirths, maceration and premature deliveries were not due to incompatibility in the Rh factor of mother and child. Some of these 48 cases, a group of 22, presented an obstetric history characteristic of that observed in haemolytic disease of the newborn. These are discussed separately below.

III. *Toxaemias of Pregnancy.*

This group of cases includes hyperemesis gravidarum, toxaemia of pregnancy, pre-eclamptic toxaemia and eclampsia.

Schwartz and Levine (1945), have pointed to the possible relation between pregnancy toxaemias and Rh incompatibility. The results of our findings in these conditions (Table III) point to the lack of any relation between Rh incompatibility and the various forms of pregnancy toxaemia, since the rate of Rh negative mothers is not significantly higher than that found in our population at random, and no Rh antibodies were found in maternal blood taken during pregnancy.

TABLE III.

Diagnosis	No. of cases	Rh negative	Percentage	Rh positive	Percentage
Hyperemesis gravidarum	5	–	–	5	100.0
Toxaemia of pregnancy	28	3	10.7	25	89.3
Pre-eclampsia	6	1	16.6	5	83.4
Eclampsia	2	–	–	2	100.0
Total	41	4	9.7	37	90.3

IV. *Other Pathological Conditions in Pregnancy.*

In this group are included cases of placenta praevia, premature separation of placenta as well as ectopic pregnancy. We have found only 1 case of an Rh negative woman among them. In this case Rh antibodies were not found in the maternal blood 8 days after operation.

TABLE IV.

Diagnosis	No. of cases	Rh negative	Percentage
Placenta praevia	8	–	–
Premature separation of placenta	1	–	–
Ectopic pregnancy	12	1	8.3
Total	21	1	4.8

As would have been expected, there is no relation between these conditions and Rh incompatibility.

V. *The Obstetrical History Characteristic of Rh Incompatibility.*

We have studied a group of 22 cases (see above), who presented a past obstetrical

history characteristic (Levine, *et al.*, 1941; Boorman, Dodd and Mollison, 1942; Cappell, 1946) of that found in foetal disease due to Rh incompatibility. In these cases one or more healthy and living children have been delivered at term, but afterwards either macerated or stillborn children had been born. In some of these cases one or more abortions preceded the present condition. In these 22 cases, only 3 were Rh negative (13 per cent). It should be pointed out that in these 3 cases signs of erythroblastosis foetalis were not found in the children, nor were any signs of isoimmunization found in the mothers. The rate of Rh negative women in this group is slightly higher than that normally observed in our population, but the increase is too low to be of any significance.

The following case is here reported to illustrate the misleading conclusions that may be drawn from the clinical history alone:

Mrs. K. S., aged 35. First pregnancy (1936) ended in spontaneous abortion in the 3rd month. The 2nd and 3rd pregnancies (1937, 1939) ended in the delivery of healthy and living children at term. The 4th pregnancy (1942) terminated by the spontaneous delivery of a stillbirth. Postmortem examination could not be performed In her 5th pregnancy (1944) the patient delivered a premature stillbirth in the 8th month. Blood typing revealed the patient to be ARh_1 and her husband BRh_1.

Immune antibodies (anti B) could not be detected in the patient's blood. Wassermann and Kahn examinations were negative and blood chemistry was normal. Postmortem examination did not reveal a cause of death.

Discussion.

In this paper we have tried to determine whether Rh incompatibility plays any role in various pathological conditions in obstetrics. The attempt to relate pathological conditions to blood group incompatibilities of mother and foetus is not new, and dates much earlier than the discovery of the Rh factor. As far back as 1905 Dienst had attempted to explain conditions such as eclampsia or toxaemia of pregnancy on the basis of maternal isoimmunization by foetal blood. Similar attempts have been made in the past by McQuarrie (1923), Ottenberg (1923), and others.

It has been observed that the great majority of cases of haemolytic disease of the newborn occur after delivery or, at most, very near term. This seems to indicate that during pregnancy foetal erythrocytes are protected against the action of maternal immune-antibodies. Such protection seems to wane near term or after delivery. It therefore does not seem probable that Rh incompatibility with maternal immunization may be a cause of termination of pregnancy during the first half of gestation.

Our findings in the first group of cases (Table I) confirm the view (Hunt, 1945; Harrison and Meacock, 1945) that a relation does not exist between habitual abortion and other forms of abortion and the Rh factor.

The possibility that Rh incompatibility may account for some of the unexplained cases of foetal damage (stillbirth, maceration) during the last trimester is naturally great. When the frank cases of erythroblastosis foetalis are excluded (Table II) no increased incidence of Rh negative individuals among women delivered of premature, macerated and stillborn infants is found.

The result of our studies in the third and fourth group of cases (Table III and IV) confirm those of Hurst, Taylor and Wiener (1946) in their recent study on the relation between toxaemia of pregnancy and Rh incompatibility.

Great stress has been laid by various authors on the characteristic pattern of the obstetric history in cases of Rh incompatibility with resultant haemolytic manifestations in the child. In our fifth group of cases, which was selected on the basis of the suggestive obstetric history, we have seen that this does not in itself serve as a diagnostic aid, and is no indication of blood group-incompatibility of mother and offspring.

The results reported here point to one conclusion. Although Rh incompatibility, both theoretically and clinically, must be present in haemolytic disease of the newborn, there is no reason to look upon it as an aetiological factor in the obstetric conditions studied in this paper.

SUMMARY.

1. The incidence of Rh negative women and the presence of Rh antibodies in them has been studied in a group of 244 cases suffering from various obstetric conditions.

2. No relationship could be found between Rh incompatibility and habitual abortion (41 cases), other forms of abortion (93 cases), stillbirths, maceration and premature deliveries (48 cases), and other pathological obstetric conditions (21 cases).

3. The results of our findings in toxaemia of pregnancy (41 cases) point to the lack of any relation between Rh incompatibility and the various forms of pregnancy toxaemia.

4. In a study on 22 cases with an obstetric history characteristic of Rh incompatibility it was found that a suspected obstetric history is no indication of an antigenic incompatibility between husband and wife.

We are indebted to Professor B. Zondek for the permission to include also his cases in this study.

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The Cause of Polar Lie

BY

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IT is the purpose of this article to give an explanation, appealing to reason, for the frequency of vertex presentation and also to suggest a cause for the foetus presenting by the breech in otherwise normal pregnancy.

Until the eighteenth century the Hippocratic teaching that the child lay as a breech until the 7th month and then suddenly underwent a spontaneous version was believed. By the time of Smellie (1750) it was thought that the presentation was maintained throughout pregnancy, but that a few breech presentations turned in late pregnancy. Smellie did much to dissipate this idea. Whitridge William's textbook of obstetrics (1923) gives an excellent account of the theories and development of thought on the subject. In 1861 both Hecker and Schultz showed that it was not really uncommon for the foetus to turn even in the later months. It is now recognized that the lie is variable in the early months, with an increasing inclination to a polar lie and a vertex presentation as term approaches. The older textbooks contained long arguments as to the aetiology of the vertex lie but most of them were expositions of the various theories that had been advanced, followed by refutations of these arguments. The reader was left unconvinced. For instance Caseaux (1869) concludes his account of the frequency of vertex presentation with "... a singular fact which does not seem, in the present state of our science, capable of elucidation by the material reasons heretofore given." Two theories held sway. For the gravitational theory Matthews Duncan (1868) and Veit (1860) held that a foetus suspended in a fluid tended to sink head first. Schatz in 1900 showed that if the solution was of the same specific gravity as liquor amnii (1.008 to 1.009) the breech end tended to sink. Seitz (1908) countered this by showing that during the last month the head increased in specific gravity and concluded that the force of gravity could account for the frequency of vertex lie. The second theory—the theory of accommodation—was supported by Dubois (1833); Simpson (1848); and Scanzoni (1853), who postulated that the foetus was irritated by the ill fit of breech presentation and moved until it was in the more comfortable fit of a vertex presentation in the uterine ovoid. Modern textbooks tend to skip the arguments and give no explanation. DeLee (1933) mentions "the law of accommodation of Pajot" which states that where an ovoid body lies free in an ovoid container the two long axes tend to become parallel. To call an observed phenomenon a law is not an explanation. Kerr, *et al.* (1944), state that the preponderance of vertex presentations is due to the ovoid foetus, with the head the narrower end, lying in the ovoid uterus wider above. He then states that "it is natural" for the child to take up a permanent position head

down. Why is it natural? He vitiates his argument by adding another reason—that the cranial end of the foetus is heavier. Eden and Holland (1931) give almost the same two reasons but use a slightly better term for an untrue assumption, by saying that the centre of gravity of the foetus lies nearer the cranial end. Ten Teachers (1931) simply state that the foetus "fits best" as a vertex. Gibberd (1938) writes that "the relatively restricted space in the uterus accounts for the frequency with which a longitudinal lie occurs."

Really thoughtful experiments and arguments were published in this Journal by Griffith in 1915. He put forward that an immersed body in fluid of less specific gravity tended to lie with its metacentre or centre of buoyancy vertically above its centre of gravity. The metacentre is the centre of gravity of the displaced fluid. By careful experiments he found that in 7 foetuses near full time the centre of gravity was nearer the breech end than the vertex and that the metacentre in the 2 foetuses he measured was 0.5 cm. nearer still to the breech end. A distance of 0.5 cm. in 2 foetuses is hardly sufficient to found a theory. From his measurements he concluded that there would be a tendency for the foetus to lie breech up and showed that the force tending to produce this movement would be a moment of about 1,383 centimetre-grammes. This is a very tiny force and is in fact 1.19 inch-pounds. This moment would diminish rapidly as the foetus turned from a transverse lie and the metacentre came more closely over the centre of gravity. Moreover in women lying in bed this force would not act; departures from the vertex lie are not more common in these. However, this article did dispose of the loose statements that the head end was the heavier end or the foetal centre of gravity was nearer the vertex.

Much greater forces than this are at work. Griffith mentions them but then goes on to develop his argument as to the physics of an immersed body. The 2 factors which I put forward as the most powerful in determining the predominance of vertex presentation are:

1. The kicking of the foetus.
2. The absence of resistance at the fundus of the uterus and its presence at the lower extremity.

The normal foetus in a position of flexion kicks by extending its hips and knees repeatedly, so propelling its breech away from its feet. The effect of this would be for the foetus to dive round and round, were it in a spherical container. The action of arm movements would be much less effective for the arms are weaker, they are folded across the thorax and covered by the knees, and the hands are so near to the centre of gravity that a thrust imparted there would tend to give little turning movement. Up to the seventh month the foetus is in a spherical container, with the result that it turns head over heels many times. As term approaches the uterus becomes broad at the fundus and comparatively narrow at its lower strait. The turning moment is, therefore, more effective when the breech is lowermost. The moment is still more effective from the presence of the pelvic brim below. There is no similar structure above. Put simply, a flexed foetus in the breech position has something to kick against and hence turn it, whereas as a vertex it has a very poor purchase. A foetus in the breech position has only to give a small kick before its feet find something to thrust against, whereas in the vertex position it must kick some inches before it finds a purchase and that is soft uterine and abdominal walls instead of lower segment and bony pelvis. The measure of this moment cannot be told unless the force of the foot thrust of a

foetus is known. By testing with a spring balance it was found that a full-time foetus could kick between 3 and 4 pounds with 1 foot. If both feet kicked together it would kick between 6 and 8 pounds, and this is borne out by the fact that with a kick a newborn baby can almost lift its weight from one's hands, though of course it cannot sustain it. Griffith's measurements showed that the centre of gravity of a full time foetus averaged 6 inches from the breech. A force of 6 pounds applied at a distance of 6 inches means a turning moment of 36 inch-pounds (42,000 centimetre-grammes) compared with the 1.19 inch-pounds (1,400 centimetre-grammes) produced at their maximum by the inert physical forces. Moreover the kicking movements do not lose their power as the foetus turns. Griffith's moment diminishes as the foetus turns until, when the metacentre is above the centre of gravity, it is reduced to zero. The feebleness of Griffith's moment is easily tested by taking a fresh, stillborn foetus and tying it by means of cotton in the normal attitude of flexion. Suspended in a bath of water with its long axis horizontal and then released, it sinks to the bottom. In a bath 2 feet deep the writer was unable to detect any tendency for the head to descend quicker than the breech and the foetus reached the bottom still horizontal. A touch with a finger and the foetus turned end for end with ease. In liquor amnii this alleged tendency for the head to descend quicker would be still less, for liquor with its slightly higher specific gravity would offer a little more resistance to turning.

It comes about then that during the first 2 trimesters the foetus turns end for end repeatedly, propelled by its feet. As the uterus assumes its decidedly oval shape during the third trimester foetal kicking will rapidly and easily convert a breech lie into a vertex, but only slowly and with difficulty convert a vertex into a breech. It follows that the inert vertex will most frequently come to lie in the narrow lower segment over the pelvic brim.

But what of breech presentation? Why do foetuses sometimes present by the breech? Long lists of causes for breech presentation are given in textbooks—contracted pelvis, placenta praevia, tumours, prematurity, multiparity, dead foetus, hydrocephaly and so on. Excluding all these cases there are still large numbers of breech presentations without such causes and the textbooks merely state that there are many cases for which no adequate cause can be found. It is the writer's thesis that the commonest cause of breech presentation is extended legs. Vartan (1940) in an article entitled "Cause of Breech Presentation" recognized extension as most commonly associated with breech lie but attributed this to "splinting" of the foetal body by the legs and hence difficulty in turning inside the uterus. This word "splinting" is frequently used in this connexion but does it really occur? It sounds reasonable, but the knees of a foetus at term are very flexible and extensible. The writer has not noticed any diminution in the mobility of the foetal body produced by extended legs when delivering a foetus in the breech position. It is the writer's opinion that with the legs extended the normal moment applied to the foetus by kicking is absent. Any kicking that does take place will be at the head end of the foetus and would tend to turn it to a breech lie.

In the primigravida the uterus is most perfectly of the ovoid shape. If this thesis is correct, extended legs should lead to breech presentation more certainly in them than in multiparae. As multiparity increases and the uterus becomes less ovoid and more spherical, the number of breech presentations produced by extended legs should be

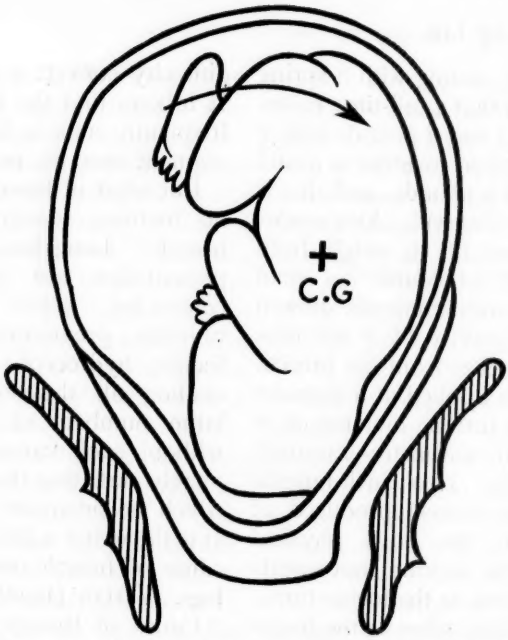

DIAGRAM 1. Weak turning moment when the flexed legs lie at the fundus.

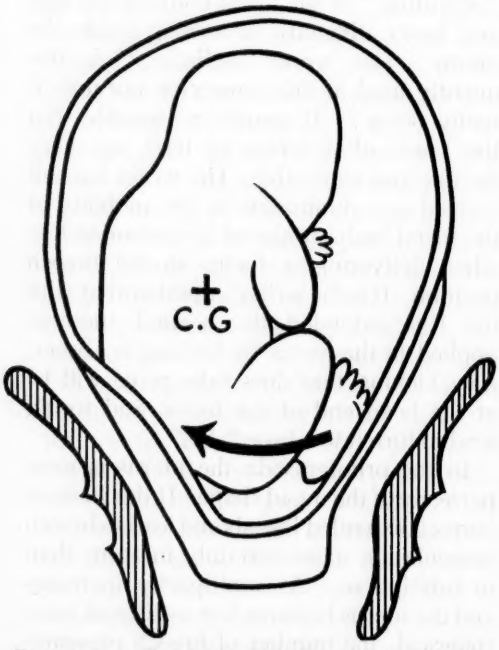

DIAGRAM 2. Powerful turning moment when the flexed legs have the closely applied lower segment and pelvic walls for purchase.

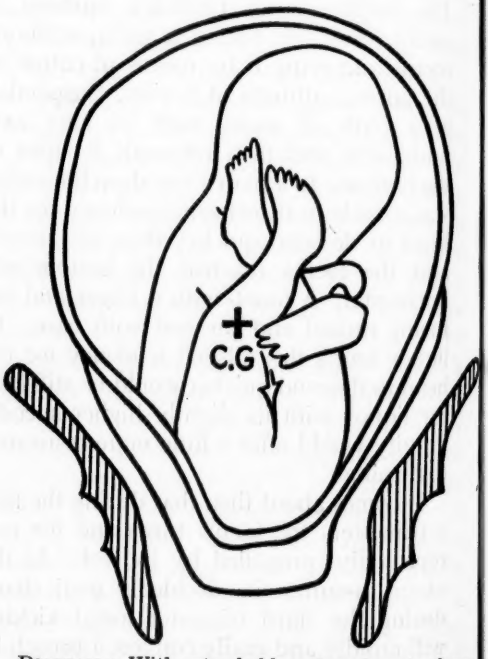

DIAGRAM 3. With extended legs there is no tendency to kick away from the breech position.

diluted by the chance occurrence of breech with flexed legs. The foetus in the multigravid uterus is under the same conditions as the foetus before 7 months. For some years the resident obstetric officers at the Princess Mary Maternity Hospital have been urged always to record the state of flexion or extension of the legs in breech presentations, but in spite of this many were merely recorded as "Breech—normal delivery", "Breech—assisted delivery" and so on. The notes tended to record extended legs only if these demanded any treatment. It is very difficult to find any reliable figures of the incidence of extended legs. Bourne and Williams (1945) state that "in women pregnant for the first time, over 50 per cent of the infants presenting by the podalic extremity have the legs extended". This true statement conveys an untrue impression. In the figures below, all those cases in which there is no record of the state of the legs are counted as having flexed legs so that the proportion of extended legs is always an underestimate. In the 7 years 1931 to 1937 there were 629 breech deliveries. Of these 309 are excluded because of gross causes for malpresentation such as contracted pelvis, twin, placenta praevia, anencephaly, hydrocephaly, etc. All cases of less than 36 weeks development are excluded.

Parity	Extended legs recorded	Flexed legs or not recorded
0	157	71
1	21	13
2	7	11
3	5	6
4	4	3
5	0	7
6	2	4
7	0	1
8	1	4
9	1	2

In first and second pregnancies extended legs preponderate in the proportion 2:1. After the second child flexed legs preponderate in the proportion 2:1. However, because of the failure to record every case fully, these figures are not very reliable.

To supply more accurate figures the X-ray films of all breech cases referred to the radiologist between 1938 and 1945 were scrutinized with the same exclusions as in the other series. The result is more in keeping with one's clinical impression that 90 per cent of breech labours in primigravidae have the foetal legs extended.

Parity	Extended legs	Flexed legs
0	30	3
1	9	1
2	5	1
3	1	1
4	0	1
5	0	0
6	0	0
7	2	0

Teaching on breech presentation usually starts with the complete breech and then considers extended legs as a complication —a "complication" which occurs in over 70 per cent of normal primigravidae with normal foetuses!

Conclusions.

1. Foetal leg movements tend to turn the foetus end for end.

2. The narrow lower pole of the uterus together with the presence of the pelvic brim makes foetal turning easy of achievement if the legs are flexed with the breech lowermost.

3. The wide, soft, upper pole of the uterus makes turning difficult of achievement if the legs are flexed with the breech uppermost.

4. As a result most foetuses present by the vertex.

5. If the legs are extended the mechanism is reversed and breech presentation is more likely.

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Central Rupture of the Perineum

A Report of a Case with a Review of the Literature

BY

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THE birth of a child through the perineum is an unusual occurrence, though by no means excessively rare. The condition is mentioned in almost every textbook of midwifery and the case reports are fairly numerous. There would seem, however, to be a place for a further case report and a full review of such literature on the subject as can at present be traced.

CASE REPORT.

Mrs. D.S. was aged 30. Her first child had been delivered in her own home in 1938. There had been a perineal tear, described by the patient as an "internal tear", which was sutured. Her height was 4 feet 11⅞ inches. Clinical and radiological pelvimetry showed the pelvis to be adequate.

Her second pregnancy was uneventful and she went into labour 7 days after the expected date of delivery. She was admitted to the labour ward of University College Hospital on January 29th, 1946. The first stage of labour lasted 3 hours. A vaginal examination was about to be made when the patient suddenly screamed that the baby was coming. The membranes ruptured and the child's head was seen to be distending the left labium majus. An attempt was made to push the head towards the midline, but this was unsuccessful, owing partly to the strong bearing-down efforts made by the patient. Almost immediately the skin of the labium and the perineum split in several places and a few seconds later the head burst through the skin and was born. The rest of the child followed quickly. The infant was a female, weighing 7 pounds 1½ ounces and was in good condition with only slight head moulding. The length of the child was 20 inches, head circumference 12½ inches, occipito-frontal diameter 5 inches, bi-parietal diameter 4 inches.

The diagram (Fig. 1) shows the appearance after delivery of the child, with the umbilical cord passing through the tear. There was complete continuity at the posterior commissure and all round the margins of the vaginal aperture. The fingers could easily be passed through the wound into the vagina, so that the left labium majus lay across the palm of the hand, bridging the gap, and apparently attached only at its anterior and posterior ends. There were also numerous superficial tears of the skin of the vulva and the vaginal

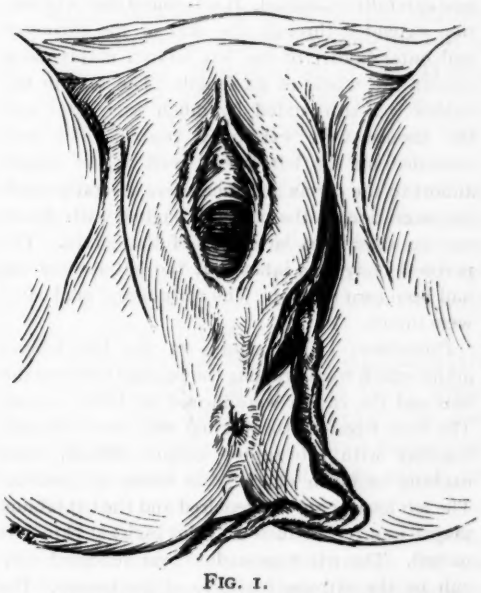

FIG. 1.

Illustrating the vulva and perineum after the birth of the child.

mucous membrane was extensively lacerated, especially on the left lateral wall.

The placenta and membranes were delivered 15 minutes after the birth of the child, through the aperture in the vaginal wall and perineum. There was no uterine haemorrhage, though bleeding from the tear became obvious 1 hour later. The patient did not complain of pain and was surprised to hear that she would have to have stitches inserted.

An injection of papaveretum ("omnopon") and scopolamine was given and an hour later the patient was taken to the operating theatre. She was placed in the lithotomy position and the tissues of the perineum and lower half of the vagina were infiltrated with procaine 0.5 per cent, and adrenaline 1:200,000. The extent of the tear was now carefully examined. It was found that a laceration extended through the skin of the perineum and outer border of the left labium majus along almost the whole of its length. The tear in the vagina was surrounded by much scar tissue and the tissues were extremely friable. The tear extended up the left lateral wall of the vagina almost to the cervix and there were several secondary lacerations in the posterior vaginal wall. There was no significant laceration of the cervix. The perineal body was intact but the left levator ani had been torn through. The rectum and anal canal were intact.

Procedure. The remains of the left labium majus which were bridging the passage between the tear and the vagina were incised for better access. The torn edges of the vaginal wall were brought together with interrupted catgut sutures, after excising as much of the scar tissue as possible. The left levator ani was repaired and the left labium majus was reconstructed. The perineal skin was united. The whole procedure was rendered difficult by the extreme friability of the tissues. The local analgesia was entirely sufficient for the whole procedure. The patient did not complain of pain and seemed unaware of the examination or the insertion of the sutures.

Puerperium. This proceeded uneventfully, except that the superficial part of the tear broke down and became slightly septic. A swab was taken and Pseudomonas Pyocyaneus was grown. Ultraviolet light was given to the perineum twice daily.

On the 14th day it was found on examination that the posterior wall was healed and intact. The perineum had broken down superficially and was gaping slightly but granulating well. It was decided to continue treatment for 3 or 4 days and then to consider resuture. One week later the perineum was almost healed. Resuture was considered unnecessary and the patient was discharged.

Postnatal. The patient attended the postnatal clinic when the child was 5 weeks old. The perineum was almost healed, but slightly deficient. There was no cystocele or rectocele.

One month later healing was complete.

Literature.

A search of the literature has revealed that central rupture of the perineum has been known to obstetricians for many years, though the earliest case reported dates from 1796. No report of a case can be found before that date.

Sir Fielding Ould in his *Treatise of Midwifery* published in 1742 does not mention central rupture of the perineum, though he does give a remarkably clear description of the operation of episiotomy, and indeed of incision of the cervix. Both operations he recommends when cicatrization of the soft parts delays or impedes delivery.

William Smellie (1774) does not describe the condition.

Matthews Duncan (1876) described central tearing or rupture of the perineum but stated that it commonly occurred without a new passage being made into the vagina, a crack appearing in the perineum or vaginal mucous membrane. The complete central rupture with perforation was a rare occurrence. He described 4 cases, but only 2 were true perforating central ruptures.

Baker Brown (1861) reported a case in a paper read before the Obstetrical Society of London in May, 1860. This was the case of a primigravida aged 20 in whom the child was born between the os vaginae and the anus. A hard, constricting band was found

along the posterior margin of the vaginal orifice. The aperture in the centre of the perineum admitted 3 fingers. The posterior vaginal commissure was divided and 2 sutures of iron wire inserted without anaesthesia and apparently without excessive pain to the patient. Complete healing took place. Baker Brown suggested that episiotomy be performed when central rupture of the perineum threatened.

The most complete review of the literature of the subject up to the year 1878 was given by Reeve. This author was able to collect 35 cases from the literature. He gives details of a personal case where he was summoned to a patient who had been delivered of her 3rd child by a midwife. He found an enormous laceration of the perineum, which had divided both sphincters of the anus, but had left the posterior vaginal commissure intact and as thick as a man's thumb. This laceration was repaired with silver wire sutures, but it broke down, and a recto-vaginal fistula remained. An attempt to cure this one year later was unsuccessful. The 35 cases collected by this author were gathered from extensive literature, including the cases described by Matthews Duncan and Baker Brown. The earliest case report that Reeve was able to trace was from Loder who reported the case in 1797, one year after its occurrence. This reference was found by Reeve in Mursinna-Osiander, *Handbuch der Entbindungs*, 1820, ii, 245.

Wilson (1878) described a case where the child was born through the perineum and the placenta through the vagina. The fourchette and sphincter remained intact.

Rogers described a similar case in 1879. This occurred in a primigravida of 24. He gives the reasons for the occurrence of the condition as a contracted state of the vaginal orifice, an inordinately long perineum or possibly a poorly curved sacrum as is found in a pelvis of the male type.

Cunningham (1879) described a remarkable case where the child escaped into the abdominal cavity through a tear in the posterior vaginal wall. Delivery was effected through the rent and *per vaginam* but death of the mother took place on the 3rd day.

Harley (1881) described the case of a primigravida of 25. Hymenectomy had been performed but the husband still complained of difficulty because "that bone" (i.e. the pubes) was still there. The first child was born through the perineum and it seemed that the low pubic arch was forcing the child backwards. A central laceration occurred with one inch of the perineum intact in front and the sphincter ani also intact. In the discussion on Harley's paper Rutherford Kirkpatrick described 2 cases and More Madden 1, all 3 having occurred at the Rotunda Hospital.

Beatty (1882) described the case of a primigravida of 24 where the child was born and the placenta followed through a central rupture which was found to be complete from side to side, but with the vagina and rectum intact.

Ribémont-Dessaignes and Lapage (1894) described the condition as fairly uncommon. They attempt to explain its mechanism on similar lines to those suggested by Rogers and give 4 drawings taken from cases.

Baudry (1894) described a case where the child's hand came out through the anus. It was replaced and the child delivered *per vaginam*. Afterwards it was found that there was a large hole between the vagina and rectum with an intact perineum.

Dodson (1906) described a case in a primigravida of 21. In a precipitate labour the child was born through the perineum, the vagina, rectum and anus remaining intact. The child weighed 6 pounds 12 ounces and after suture of the tear there was a good recovery.

Seyffardt (1922) described a case where the child was born through the perineum, while episiotomy was being considered. It was found that the perineum was torn through to the anus. The rectum was lying free but intact. There was a deep tear in the posterior vaginal wall, exposing the peritoneum. The tear was repaired and recovery was complete in 14 days.

Scheven (1923) described a case in a primigravida of 21. Here the child was born through a rent between the vagina and anus but the rectum remained intact.

Karlin (1927) described a case of central rupture of the perineum and quoted the literature up to the year 1926; all from German sources. He quoted a paper by Hagen (unobtainable) who gave the findings in 39 cases from the literature. These are tabulated as follows:

Age	
17–25	16
26–30	13
30–34	2
Parity	
Primigravidae	27
Under 25 years	16
Over 25 years	9
Multigravidae	8
Soft parts	
Narrow or rigid vulva	15
Long perineum	25
Hypoplasia of vulva	2
Normal perineum	1
Gaping perineum	4
Scarring of soft parts	6
Pelvis	
Narrow pubic arch	8
Contracted pelvis	9
Normal pelvis	7
Presentation	
Vertex presentation	21
Vertex with prolapse of limbs	3
Contractions	
Violent uterine contractions	23

Sachs (1926) while not describing any cases discussed the mechanism of production of central rupture of the perineum. The condition occurs either in nulliparae or in cases where there has been a previous tear of the perineum or an operation. Delivery is sometimes protracted, sometimes precipitate. In one variety the tissues are rigid, a crack occurs in the perineum and the child escapes through the eventual central laceration. Here labour may be long. In a second variety precipitate delivery takes place and the force of the contractions drives the child through the perineum. In a third variety the child's head escapes out of the vagina into the fascial space surrounding it and eventually bursts through the skin of the perineum or the surrounding structures.

Sachs quotes the opinion of Zangemeister who suggested that in these cases the perineum is elongated and the frenulum lies far forward. The vaginal introitus is not in line with the descent of the head which comes to lie on the perineum rather than on the vaginal walls. Over-stretching of the vagina in the long axis and rigidity of the soft parts are contributing factors.

Naylor (1926) described a case in a primigravida of 36. During the second stage of labour a bleeding spot appeared near the anus. Central rupture of the perineum followed and liquor amnii escaped. An episiotomy was immediately performed and a child weighing 9½ pounds delivered. The anal sphincters and rectum were intact.

Bussalay (1927) described a case where a child, placenta, etc., were delivered through the perineum. He ascribes this to malformation of the ostium vulvae and to excessively powerful uterine contractions.

Duthie (1928) gives a clinical note of a case in a primigravida of 37 who was delivered by a midwife. Precipitate delivery took place through a tear in the perineum. The child was not unduly large.

Afterwards a tear 3 inches long was found to the right of the midline, with a large tear in the posterior vaginal wall. The posterior vaginal commissure was intact.

Tindal and MacLennan (1930) reported a case which they described as a "unique case in the history of perineal tears". The baby was born through an extensive perineal tear, involving the posterior and lateral vaginal walls, levator ani and transversus perinei. The anal sphincter was not involved.

Guglielmi (1932) stated that central perineal laceration, though not very frequent, is less rare than is generally supposed. Varying mechanisms are described. The condition should be avoided if possible by prompt episiotomy. He recommends immediate repair.

Meyer (1935) described 2 cases. The first was a patient aged 28 who had had an episiotomy in her previous labour. In the 2nd labour the child was born through the perineum. In the 2nd case the patient was a primigravida of 20. At the height of bearing-down, the recto-vaginal septum split and the child's right foot came through the perineum. The child was born spontaneously. The vulval orifice was intact and the laceration admitted 3 fingers.

Leclerc (1935) described a case in a girl of 19. The whole perineal body was perforated between the vulva and the anus with the posterior commissure intact. He recommends episiotomy and then suture.

Kovacs (1942) described the condition as "paracentral tear of the perineum" and quoted theories of the causation of the condition from various authorities. He mentions von Bigelow, Klein and Stoeckel as ascribing the condition to the fact that in these cases the perineum is too high. According to von Münster and Mandelstamm a narrow outlet is responsible. Stortfeld and Mathei ascribe the condition to a scarred condition of the perineum and Fergusson and Seidentopf to rigidity from previous tears. Kovacs suggests that these various factors may all play a part. In a series of 16,000 births collected over 10 years, central rupture of the perineum occurred on only 4 occasions, an incidence of 1 in 4,000 labours. The mechanism suggested by Kovacs is that the foetal head comes to lie in the recto-vaginal space and bursts out of it through the perineum. He suggested a congenital origin and illustrates 2 sites where congenital weaknesses of the pelvic floor may exist. One anteriorly in the triangle formed by the bulbo-cavernosus, ischio-cavernosus and transversus perinei, and the other posteriorly, behind the transversus perinei, and in the triangle formed by it with the levator ani and gluteus maximus. An illustration is given of the latter type of pelvic hernia occurring in a woman of 30. Kovacs believes that these herniae are of atavistic origin, resulting in a congenital weakness of the pelvic fasciae and muscles.

Two papers dealing with central rupture of the perineum have appeared but are unobtainable in this country or in the Army Medical Library, Washington, D.C., U.S.A. These were by Tolosa and Pawel (1940) of Brazil, and by Gerinshteyn (1940) of Russia.

Many general descriptions of the condition have appeared, some detailed and illustrated, though in the majority of obstetrical textbooks the subject is dealt with in a few lines and is described as rare or unusual.

Hermann (1910), in *Difficult Labour*, gives a fairly detailed description with several illustrations, taken from Ribémont-Dessaignes and Lapage. He quotes the opinion of Mme La Chapelle and Matthews Duncan that it is more common, even when a central rupture has taken place, for the child to emerge through the proper orifice.

Zangemeister (1927) in his *Lehrbuch*

der Geburtshülfe gives the incidence of central rupture of the perineum as 0.03 per cent, or 1 in 3,000 labours.

Munro Kerr (1937) refers briefly to the condition, but states that in many cases the rectum is involved in the tear. It seems from the reports of the literature that this complication is rather unusual, and that the rectum and anal canal often escape.

He also describes a case where a primipara was brought to the hospital with the foot of the child protruding through the anus, although no attempt had been made to deliver the child.

Stoeckel (1938) in his *Lehrbuch der Geburtshülfe*, describes the following as aetiological factors in the production of central rupture of the perineum: high perineum, steep pelvic angle, narrow and rigid introitus, especially from old tears, friability of the posterior vaginal wall and the adoption of the squatting position. He notes that a hand or foot of the child may emerge first even with a vertex presentation.

Conclusions.

The mechanism by which the child and placenta escaped through a rent in the posterior vaginal wall and perineum seems to be fairly easily explained in the case which has been described. Little is known about the patient's first confinement, but she was confined in her own home, was told that she had had an internal tear, and sutures were inserted by a midwife. It seems likely that these sutures were inserted through the skin only and that scarring resulted in the perineal area with a weakness in the lower part of the posterior vaginal wall. In the 2nd labour, delivery could be described as precipitate. As the head came down on to the perineal body, the rigidity of the previously sutured area prevented the usual distention of the vulval orifice. The weak area in the posterior vaginal wall gave way, and the child's head came to lie in the fascial space posterior and lateral to the vagina. The force of the uterine contractions then drove the head through the skin of the perineum and that overlying the left labium majus. The child emerged very much to the left side, and it is possible that a congenital hernia or weakness of the pelvic floor, as described by Kovacs (1942), was present in this case.

Radiological examination of the pelvis did not reveal any evidence of contraction of inlet or outlet nor any abnormal configuration of the sacrum. Pelvic contraction does not seem to have been a predisposing factor in this case.

Obviously this patient should have had an episiotomy as soon as the true state of affairs was revealed. It is unfortunate that delivery was so rapid that skilled aid could not be obtained in time for this to be performed, as it is probable that the very extensive laceration of the vaginal wall would have been prevented by this means.

It is of further interest to note that local analgesia, combined with premedication, was entirely satisfactory for the repair of this extensive laceration.

Summary.

A case is presented where spontaneous delivery took place through the perineum, after extensive tearing of the posterior and lateral vaginal walls. The patient had had a perineal tear in a previous confinement. The bony pelvis was normal in size. The literature on central rupture of the perineum is reviewed. It is concluded that when such laceration is threatened, episiotomy should be performed without delay.

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Rupture of the Rectus Abdominis Muscle during Pregnancy

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THE relative rarity of this complication of pregnancy and labour is stressed by Thomas,[1] and Torpin,[2] in recently published case reports, indicating that only 32 recorded cases appear in the literature. This communication, therefore, seeks to place on record the clinical and pathological details of another instance of this complication which occurred at the Brisbane Womens's Hospital in June 1939, and to call attention to a report of a similar case which was omitted by Torpin in his otherwise comprehensive review of the literature.

The high maternal mortality (13 per cent) resulting from this condition as a complication of pregnancy[2] is a reminder of the need for early and correct diagnosis, for it is probable that this figure would have been very different if early haemostasis had been effected and modern transfusion facilities used. In only 9 of the 32 cases reported was the correct diagnosis made prior to operation. It is probable that this was due to failure to consider the possibility of such a lesion rather than to difficulty in eliciting the more characteristic physical signs. Careful examination of any atypical features presenting in a case of concealed accidental haemorrhage may possibly lead to a correct diagnosis of haematoma of the rectus abdominal muscle. Personal experience suggests that the condition may be simulated by acute necrobiosis of a uterine myoma, axial torsion of the pregnant uterus,[3] haemorrhage into an ovarian cyst with twisting of its pedicle, and acute hydronephrosis.

CASE RECORD.

Mrs. F.W., aged 36 years, was pregnant for the third time. Her previous obstetrical history did not contain any significant features; both infants had been born at term and there had not been any miscarriages. (Physical examination subsequently revealed a systolic and diastolic murmur at both aortic and pulmonary areas; the blood Wasserman reaction was negative.)

At the time of admission to the Brisbane Women's Hospital at 10.45 p.m. on June 24th, 1939, her pregnancy had advanced to the 34th week. It was learned that the patient had had a troublesome cough for several weeks and that during the previous 24 hours it had been associated with distinct pain over the right side of the abdomen whenever a bout of coughing occurred. Three hours prior to admission she had been seized with persistent pain in this region, which had now become very tender. She had felt faint and expressed the opinion that the abdomen was swollen on that side.

On examination the patient was pale and somewhat distressed. The pulse-rate was 120 and the temperature, although normal on admission, registered 97.8°F. a few hours later. Her urine was free of albumin and the blood-pressure was 125/70 mm. Hg. The uterus was enlarged to the size of a 34 weeks' pregnancy, and external ballottment of the foetal head could be demonstrated without difficulty above the pelvic brim. The right side of the abdomen, however, from the costal margin to the iliac fossa was the site of a tender, moderately firm, elongated tumour. Palpation of the uterus through the left rectus

muscle showed it to be of normal consistency. Peri-umbilical staining with haemaglobin was absent. The abnormal maternal heart sounds referred to were noted; there were numerous rhonchi on auscultation of the chest. Erythrocytes numbered 2,780,000 per c.cm., and the haemoglobin content was estimated as 50 per cent.

A diagnosis was made of haematoma within the right rectus sheath following partial rupture of the right rectus muscle. Morphine and atropine were administered and codeine in a linctus was given at regular intervals in an endeavour to control the coughing attacks, and a firm abdominal binder was applied. Whilst a compatible blood donor was being sought a period of expectant treatment was followed. On the following morning the clinical picture was not very different from that presented on admission. By 2 p.m., however, the area of swelling and tenderness had extended to the right flank and the degree of tenderness had increased. Subsequently the pulse-rate rose to 168 and the blood-pressure fell to 100/55 mm. Hg.

Further conservative treatment was therefore abandoned and under nitrous oxide, oxygen and ether anaesthesia the right rectus sheath was opened by a paramedian incision approximately 8 inches long. Extensive laceration of the fibres of the right rectus muscle had occurred just below the level of the umbilicus. Almost half the width of the muscle belly on its medial side was involved, but no definite line of rupture could be demonstrated. Blood was still oozing from the ragged muscle edges and spurting feebly from 2 branches of the inferior (deep) epigastric artery; these were secured.

An extensive haematoma consisting chiefly of recent blood clot had formed between the muscle and its posterior sheath superiorly and immediately anterior to the peritoneum and fascia transversalis, inferiorly. Virtually the whole muscle belly had been displaced forward by this huge clot which extended upwards to the right costal margin, down to within 2 inches of the symphysis pubis, and laterally well out towards the flank. The amount of blood clot removed was sufficient to fill 4 standard size kidney dishes.

The space created by the haematoma posterior to the medial half of the rectus muscle was packed with gauze, which was then lead through a wide-bore rubber tube placed in the lower end of the wound. It was anticipated that a pad incorporated in a firmly applied wound dressing would help to obliterate the more lateral portions of the haematoma cavity. The peritoneal cavity was not opened and the incision was closed, using an "anchor dressing" in conjunction with the tension sutures. Replacement therapy using saline by the intravenous route was commenced and this was followed by a transfusion of Group O blood. The pulse-rate was 140 per minute and the general condition of the patient was fair when she left the theatre. Oxygen was administered by an intranasal catheter and nursing was carried out with the patient in a semi-sitting position as soon as she had recovered from the anaesthetic. The administration of sulphapyridine in full dosage was commenced and an expectorant mixture was given in place of the linctus.

On June 26th, however, the patient was still very ill; her temperature had risen to 100.6°F. and the pulse-rate varied from 130 to 140 per minute. Some upper abdominal distension was present. Auscultation of the chest revealed abundant moist sounds. Subsequently signs of peripheral circulatory failure developed with a rapid, irregular pulse, falling blood-pressure and intense pallor. The patient died during the day.

Autopsy was performed and it was then learned that in addition to the findings made at operation, the haematoma had infiltrated into the right parametrium, separating the layers of the broad ligament. Early pneumonic consolidation was present in the upper lobe of the left lung and both lower lobes were intensely congested. No abnormal changes had occurred within the uterus (Caesarean section had been performed immediately after the death of the mother, but the infant was stillborn).

Discussion.

Quite the best account of the condition of haematoma of the rectus abdominis muscle comes from the pen of Cullen and Brödel.[4] The causes are listed as muscular exertion, pregnancy, typhoid fever, influenza or influenzal pneumonia, heart disease, haemorrhagic diathesis, gall bladder disease, tetanus, syphillis and occasionally, by direct violence. When

seen in association with typhoid fever and influenza, extensive waxy degeneration of the rectus muscle, "Zenker's degeneration," has been observed. In such cases the muscle is brittle and easily torn. When haematoma of the rectus muscle has developed as a complication of pregnancy however, a history of trauma or abnormal muscular stress appears to be more common that a record of previous debilitating or constitutional disease. Thus in Torpin's series only 1 case was associated with typhoid fever, and 2 with influenza, whilst 15 cases had a cough of varying severity and duration, 5 developed the haematoma during the course of labour and in 2 cases the lesion followed a fall. The same type of observation is made in the more recently reported cases, 1, 5.

But however significant these factors may appear as a precipitating cause in the production of the haematoma, the frequency of cough as a symptom during otherwise uneventful pregnancies, and the rarity of rectus injury as a complication of labour, suggest the presence of some, as yet unknown, predisposing factor of aetiological importance. Whilst evidence of previous debilitating disease is rare, multiparity is the rule and the complication is essentially one of late pregnancy when the recti are stretched over the enlarging uterus.

Yet unless we are to believe that rupture of the rectus abdominis in multiparae approaching term or in labour is a purely accidental and fortuitous occurrence (as, of course, it may be), these observations have no real significance of an aetiological nature. Is there any further line of approach in the search for more specific predisposing factors? Bourne[6] has recent-expressed the thought that must have been in the minds of many obstetricians in reference to the varying effects of pregnancy on the subsequent structure and tonus of the anterior abdominal wall. He states: "a first pregnancy may be followed by a long, perhaps permanent, period in which the abdominal wall is slack and toneless, whilst on the other hand some women who have had many children manage to preserve a good abdominal contour. There is some factor, deeply inherent in the individual, which influences muscle tone and which confers on him or her their characteristic type. This has nothing to do with muscular development or strength." Bourne suggested that an endocrinal factor was probably involved.

It may be that the same factors that determine which patient shall suffer permanent damage to the abdominal recti (in the absence of hydramnion or twin pregnancy) are also operative, though of course to a greater extent, in predisposing certain multiparae to the formation of haematoma in the presence of a precipitating cause. Several authors have put forward the suggestion, which in some instances has been confirmed, that the development of small haematomas within the rectus sheath during pregnancy is not an uncommon occurrence. Thus Hobb's case,[7] a 6-para who suffered a fatal haemorrhage into the rectus sheath during the 39th week of her pregnancy was found at autopsy to have a sausage shaped tumour distending the left rectus sheath from the pubes to the costal margin. There was a large ragged tear on the posterior surface of the muscle belly at the junction of its middle and lower thirds, and 3 pints of blood clot were removed. There was evidence of previous small tears with old blood clot attached in the upper portion of the muscle. Torpin expresses the opinion that an appreciable number of haematomas of the rectus muscle in pregnancy and labour are small, undiagnosed and consequently unreported.

From the point of view of diagnosis Cullen states that haematoma of the rectus muscle has simulated nearly every form of acute abdominal lesion. In addition to the conditions already referred to in this paper he suggests the possibility of confusion with abdominal hernia, acute appendicitis, thickening of the sigmoid colon and gall bladder disease. Staining of the peri-umbilical abdominal fat is likely to be present only when rupture of the rectus sheath has occurred. In the more obscure cases incision of the rectus sheath is necessary before the true nature of the condition can be recognized.

Dixon Hughes'[8] case, which was the 1 omitted from Torpin's series, is chiefly of interest from the point of view of diagnosis. The patient was an 8-para in the 38th week of her pregnancy. Again a severe cough was prominent in the history. The possibilities considered had been degeneration in a myoma, accidental haemorrhage, twisted ovarian cyst and hydronephrosis. A urogram revealed a large renal calculus and a hydronephrosis. The latter was drained by ureteric catheterization, but the tumour remained. Subsequently a para-rectal incision was made and an amount of blood clot sufficient to fill a large kidney dish was removed from behind the right rectus muscle. A branch of the inferior epigastric artery was secured. The patient did well.

Consideration of the anatomical aspects of rupture of the rectus abdominis reveals several points of interest. Although the lesion may occur in any part of the muscle it is usually found below the level of the umbilicus where, for the greater part, the posterior sheath is missing, so that the blood lies between the muscle and the peritoneum. It is because of the peritoneal irritation resulting from a haematoma in this site that symptoms simulating various acute abdominal conditions have been described. Actual rupture into the general peritoneal cavity is most uncommon and the surgical treatment of haematoma of the rectus sheath should not entail opening into this cavity.

The reason for the higher incidence of these lesions within the lower half of the rectus sheath is not immediately obvious. Walmsley,[9] writing on the anatomy of the anterior abdominal wall, points out that the recti (and in man the external obliques), through their attachment to the thorax above and the pelvis below, are concerned in the maintenance of posture and antero-posterior movements of the trunk. The hypogastric region, however, since it lies between the iliac bones, and is in this sense part of the pelvis and moving with it, does not take part in these movements. It is in this "skeletal" area that the rectus is unsegmented and largely unattached to the sheath except along the linea alba.

I would suggest that in the unsegmented and unattached condition of the rectus muscle in the hypogastrium may lie the explanation of the greater incidence of rupture within this area. Ligget's[10] case is worthy of mention because of the atypical site of rupture. The fibres of the right rectus muscle had been torn opposite the tip of the 9th costal cartilege with the production of a localized tender swelling in the right hypochondrium, but no symptoms suggestive of an abdominal emergency. The patient, who was 7 months pregnant at the time of the incident, continued to term after the clot had been evacuated and was subsequently delivered *per vaginam*.

Reviewing briefly the matter of treatment, it is now evident that an expectant policy is rarely the correct one. Because of the anatomical considerations obtaining, there is little to prevent a subumbilical haematoma from extravasating widely with peritoneal irritation and shock aggravating the symptoms arising from the haemorrhage itself. On the other hand, a

small well-localized tumour in the upper portion of the rectus, though correctly diagnosed as a haematoma, may well be treated conservatively in the absence of any increase in size.

Summary and Conclusions.

1. A fatal case of rupture of the rectus abdominis muscle, occurring during the 34th week of pregnancy, is recorded.

2. Aetiological factors in the production of this type of lesion, as a complication of pregnancy and labour, are discussed.

3. The literature on the subject is reviewed with special reference to diagnosis, anatomical considerations, and treatment.

4. Suggestions in regard to aetiology and conclusions in respect of treatment are offered.

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An Uncommon Sequel of Secondary Rupture of the Uterus

BY

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DANGER of secondary rupture of the uterus led to the dictum "once a Caesarean section, always a Caesarean". Secondary rupture may be so unobtrusive as to merit the designation "silent". Silent rupture may give great difficulty in diagnosis.

According to Berkeley *et al.*,[1] some secondary ruptures occur in pregnancy, but most occur early in labour. Some occur before the onset of labour, even forestalling obstetric presentiment,[2] others—the more predictable—occur during the course of labour, or in the process of extracting an aftercoming head, or in removal of an adherent placenta.

Silent rupture occurred in the case now reported, and the sequel of this rupture is worthy of record.

Mrs. C. R., aged 36, 6-gravida.

Previous obstetric history. The first 3 were normal pregnancies with spontaneous deliveries. The 4th pregnancy was terminated 3 days before term by classical Caesarean section for central placenta praevia on April 4th, 1940. The 5th pregnancy reached term and a 3-hour labour ended on May 5th, 1943, in spontaneous delivery of a 7¾ pounds baby.

Present pregnancy. The patient had arranged to have her confinement in her own home, and the expected date of delivery was January 17th. All was well until January 16th, when the patient experienced tumultuous foetal movements. Thereafter no sign of life was felt. She was seen at home by her medical attendant who apparently heard foetal heart sounds and assured her that the foetus was still alive. A period of 7 weeks elapsed and the patient still did not go into labour. Two days of slight haemorrhage then occurred and on suspicion of recurrent placenta praevia the woman was sent to hospital.

On admission her general condition was good and the slight bleeding stopped in 24 hours. The abdomen was free from tenderness. There was some excess of liquor and the foetus was mobile from transverse to breech. Foetal heart sounds could not be auscultated. Examination of the blood showed a negative Wassermann reaction, and blood grouping showed Group A, Rhesus positive (subgroup Rh_1). The husband also belonged to Group A, and to the identical Rhesus subgroup. X-ray of the pregnancy revealed Spalding's sign which confirmed clinical suspicion of foetal death.

Treatment. The risk of secondary rupture seemed worth taking in view of the intrauterine death. Accordingly the lie of the foetus was made longitudinal by external version and the membranes ruptured by the use of a Drew Smythe catheter. Meconium blocked the catheter when a pint of liquor had been withdrawn and the catheter was removed. Oral Stilboestrol, and intramuscular oestrogen were given to sensitize the uterus.

Progress. The patient remained without pain of any kind for 18 days. Five days after induction the temperature and pulse-rate became elevated and simultaneously the meconium-stained liquor which had been trickling gave place to free loss of offensive discharge. A full course of sulphathiazamide was prescribed and low-pressure vaginal irrigations given at 4-hour intervals. The 6th and 7th days were less febrile, but on the 8th intramuscular penicillin injections at 3-hour intervals were given as there was recurrence of febrile disturbance. The cervix was examined at this time and found to be 1 cm. dilated. Penicillin therapy was continued during the 9th, 10th, 11th and 12th days. By the 13th day the general condition had somewhat improved and under intravenous anaesthesia the cervix was dilated with difficulty to 2½ cm. and

a leg was brought down. A fillet was attached to the leg and a 2-pound weight applied. The general condition improved during the 14th to 17th days, but pains did not occur and advance of the leg was not observed. On the 15th and 17th days a pint of blood was transfused.

Delivery. On the 18th day some advance of the leg was noticed although there was still no pains. With slight additional traction and pressure on the fundus, the putrid foetus escaped *per vaginam*. The birth was followed by a despumation in which the placenta and 3 pints of foul blood-stained greenish fluid escaped. Ergometrine was given intramuscularly, but there was no postpartum haemorrhage. On the following day a 3rd pint of blood was transfused.

Puerperium. On the 5th day following delivery, the temperature rose again to 104°F. and the patient complained of pain and tenderness in the right epigastrium. On palpation of this region a mass was felt with hard sharp edges just below the skin. With gentle pressure crepitus was elicited. Radiography revealed the mass to contain bones derived from the foetal skull (Fig. 1). A period of 4 days was allowed for further penicillin treatment and for localization of sepsis in the abdomen. On the 9th day of the puerperium, the mass was more superficial and sequestrectomy was undertaken. This was effected under local infiltration anaesthesia supplemented by inhalation anaesthesia during actual removal of the bones.

Operation Notes. A 3½-inch upper right rectus incision was used. The rectus was split over the apex of the mass. The peritoneum was found to be congested and when incised grey-green pus escaped. The abscess had two loculi, one anteroposterior and the other transverse. The line of the incision was common to the planes of both loculi which were disposed at a right angle. From the anteroposterior loculus one frontal bone and one parietal bone were removed, and from the transverse came the other frontal bone. Thereafter a free escape of greenish pus occurred. A rubber drain was inserted to the depth of each loculus and the abdomen closed. Penicillin was instilled through the drainage tubes into the abscess cavity twice daily for 4 days, after which the tubes were removed. The patient made a rapid recovery and was ready for discharge to a convalescent hospital 11 days later. Three weeks later she was allowed home, on condition that she reported for follow-up.

In order to determine the extent of healing of the rent in the uterus, a hysterosalpingogram was made 8 weeks after confinement (Fig. 2). Rotary displacement of the uterus was noted but there was no " spill " through a uterine fistula as might have been expected.

Twelve weeks after confinement there has still been no menstruation, nor has there been abdominal discomfort suggestive of menstruation into the abdomen. The patient is very well, the abscess scar is sound, but there is still a minute discharging sinus in the wound. She has wisely consented to have menstruation stopped by X-ray therapy.

Discussion.

A case of silent secondary rupture of the uterus is recorded. When first seen in hospital the pregnancy had exceeded by 8 weeks the time for repeat elective section,[3] and intrauterine death had taken place. Delivery was eventually effected 10 weeks after term.

In view of the intrauterine death it was decided to incur the risk of secondary rupture, about 2 per cent according to Delfs and Eastman,[4] by attempting vaginal delivery. Unfortunately, rupture took place and was of the silent variety. As in 25 per cent of such cases,[4] shock and pain were absent. Tenderness over the uterus may have been present but it was discounted as due to putrefaction. True labour pains did not occur, indeed at one stage it appeared that it would become necessary to dilate the cervix and perform embryotomy.

From the localization of the bones as found at sequestrectomy, it is presumed that the bones passed through the rent together. Their escape was aided by their serrated edges, by the presence of putrefaction, and by painless detumescence of the uterus. It is a matter of conjecture whether the bones passed through the uterus

FIG. 1.
Radiograph showing sequestra in abdomen.

FIG. 2.
Hysterosalpingogram eight weeks after delivery.
F.F.

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before the leg was secured *per vaginam*, during the spell of traction on the leg, during delivery of the aftercoming head, or in the early puerperium. It seems possible that the "artificial" delivery *per vaginam* may have arrested a "natural" expulsion of the foetus into the abdomen, but more probable that the bones were left in the uterus after delivery and their escape aided by the prophylactic administration of ergometrine. Migration of foetal parts towards the surface of the abdomen is not uncommon in secondary abdominal pregnancy,[5] and could presumably obtain in this instance.

Conservative treatment has been advocated by Herbert Spencer,[6] Munro Kerr,[7] Naguib Mahfouz Bey,[8] and others in the treatment of rupture of the uterus. The mortality with conservative measures is surprisingly low.[7] It came to be applied indirectly in the case recorded and the result has been excellent considering the gravity of the sequel.

If the gravid uterus containing the dead foetus had been left alone it is possible that uterine rupture would still have supervened and been followed by formation of a lithopaedion.

Conclusion.

Recovery of foetal parts from the abdomen has been reported in extrauterine pregnancy. The case recorded illustrates this as a possible sequel of silent rupture of the uterus.

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The Effect of Oestrogen (Stilboestrol) on the Formed Elements of the Blood in Women*

BY

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LARGE doses of oestrogens exert a profound influence upon the blood picture of some species of animals. Arnold and co-workers (1936, 1937) found that large doses of oestrogen suppressed haemopoietic processes to such an extent that death resulted. Balo and Purjesz (1937), Bareuther and Schabbel (1937), Tyslowitz (1938) reported gradual anaemia, haemorrhagic purpura and leucocytosis followed by a leucopenia in dogs after the administration of natural oestrogens. Tyslowitz (1939), Arnold (1939), and MacBryde *et al* (1940) repeated the above experiments using diethylstilboestrol (stilboestrol) and obtained similar results.

Crafts (1941) repeated the experiments with natural and synthetic oestrogens in dogs and monkeys and found in the dog that stilboestrol caused a marked neutrophilia followed by a decrease in the young neutrophils, anaemia, and a decrease in haemoglobin. Daily doses of 5 mg. of alpha- or beta-oestradiol produced similar results. In monkeys Craft reported that 10 mg. doses of stilboestrol did not produce the condition found in dogs but there was a slight anaemia. Even fourfold dosage of stilboestrol per kg. of body weight in the monkey did not produce the blood picture found in dogs with 5 mg. daily doses of the same oestrogen.

Tyslowitz (1941) studied the blood picture in some of the monkeys in the Carnegie colony in Baltimore and stated that "the blood picture suffered little change" when these animals were treated with large doses of oestrogens.

Shute (1946a) states that women who have prolonged bleeding and coagulation time usually have high blood oestrogen levels and that vitamin E corrected this. He also quotes Castrodale and his associates and Tyslowitz and his co-workers that the administration of oestrogens to dogs decreases the blood platelets even to purpuric levels. Shute (1946b) concluded that stilboestrol would lower the platelet count and cause purpura in women receiving stilboestrol, so it was thought a study of some of the formed elements of the blood in women should be reported because stilboestrol is being used more and more.

Methods.

One hundred and sixty-three pregnant and non-pregnant women coming to the Out-patient Menstrual Disorder Clinic, Jefferson Davis Hospital, were given various dosages of stilboestrol by mouth and intramuscularly for various periods of time from 1 week to 1 year. In some the dose was increased every 2 to 6 weeks.

In some patients stilboestrol was stopped for 4 weeks to 6 months and then started again.

Blood platelet, red-blood cell and white-blood cell counts and haemoglobin deter-

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minations were made before, during and after stilboestrol was given.

Results.

In 93 platelet counts before stilboestrol medication the average was 268,124.

In 639 platelet counts during stilboestrol medication the average was 261,756. These patients had daily stilboestrol dosages from 0.125 to 2,000 mg.

In 168 platelet counts after stilboestrol medication the average count was 267,380. These patients had total stilboestrol dosages from 0.7 to 111,000 mg.

In 211 red-blood counts before stilboestrol medication the average was 3,677,109.

In 861 red-blood counts during stilboestrol medication the average was 3,578,850.

In 229 red-blood counts after stilboestrol medication the average was 3,616,900.

In 209 white-blood counts before stilboestrol medication the average was 6,213.

In 689 white-blood counts during stilboestrol medication the average was 7,058.

In 194 white-blood counts after stilboestrol medication the average was 6,851. These patients had total dosages of stilboestrol from 0.7 to 111,000 mg.

In 201 haemoglobin determinations before stilboestrol medication the average was 71.8 per cent.

In 688 haemoglobin determinations during stilboestrol medication the average was 74.6 per cent. These patients had daily dosages of stilboestrol from 0.125 to 2,000 mg.

In 192 haemoglobins after stilboestrol medication the average was 76.9. These patients had total dosages of stilboestrol from 0.7 to 111,000 mg.

Table I shows the number of mg. of stilboestrol taken and the number of patients receiving those amounts.

Table I.

No. of patients	Total No. of mg. of stilboestrol
26	0.7 to 25
20	26 to 50
11	51 to 100
10	101 to 150
4	151 to 200
4	201 to 250
1	251 to 300
2	301 to 350
2	351 to 400
2	401 to 450
3	451 to 500
3	501 to 550
4	551 to 600
1	601 to 650
1	650 to 700
3	701 to 1000
7	1001 to 2000
4	2001 to 3000
5	3001 to 4000
5	4001 to 5000
3	5001 to 6000
4	6001 to 7000
5	7001 to 8000
2	8001 to 9000
4	9001 to 10,000
10	10,001 to 15,000
3	15,001 to 20,000
3	20,001 to 25,000
2	25,001 to 30,000
4	30,001 to 40,000
2	40,001 to 50,000
1	50,001 to 60,000
1	60,001 to 70,000
1	70,001 to 111,000
163	

Discussion.

In dogs large doses of stilboestrol caused marked changes in the blood picture while in monkeys there was little, if any, change.

In our series in women the blood picture was not altered from the control before and after stilboestrol, even when a total dosage

of 111,000 mg. of stilboestrol was given over a period of 1 year.

We might fairly conclude that stilboestrol produces no changes in the haemopoietic process in women. The platelet count was approximately the same before, during and after stilboestrol.

No patients developed purpura haemorrhagica, nor did the abdominal or perineal incisions bleed more in those undergoing operation.

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The Familial Incidence of Adrenal Hypertrophy and Female Pseudohermaphroditism

BY

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THE cases described in this paper are those of 2 female pseudohermaphrodite infants occurring in the same family. At the death of the first the mother was advised to have a further pregnancy because it was considered unlikely that this malformation would recur. When it was exactly reproduced in the subsequent child it was thought of value to determine how frequently this defect is familial.

Two types of pseudohermaphroditism should be distinguished. The male pseudohermaphrodite is of male genetic constitution, but factors operating during development modify growth in the female direction. There is therefore hypospadias of varying severity, often maldescent of the testes and effeminate bodily form. There is rarely any anatomical abnormality of the endocrine glands. Male pseudohermaphroditism is well recognized to be inherited and Witschi (1939), reviewing the literature, records 11 families with a total of 42 male pseudohermaphrodite individuals.

In the female pseudohermaphrodite the genetic constitution is female but hormonal influences during intra-uterine life lead to masculinity. Individuals with this defect show hypertrophy of the clitoris, varying degrees of maldevelopment of the vagina and as growth proceeds a masculine bodily form. The cortex of one, or more commonly both, adrenals is hypertrophied.

Although these 2 types of pseudohermaphroditism are genetically and developmentally quite different the distinction between them may be very difficult, and in many cases impossible, without a laparotomy. It is not uncommon for a pseudohermaphrodite to be brought up as a member of the wrong sex, or for the sex to remain in doubt throughout life.

The present cases are typical examples of female pseudohermaphroditism. The infants were the 2nd and 3rd children of normal parents who were not related to each other. Similar abnormality could not be traced in the family. The 1st child is a normal female, now aged 7 years.

CASE 1. The child weighed 8½ pounds at birth and was considered to be a female because there was some loss of blood from the vulva during the first few days of life. There was marked hypertrophy of the clitoris and no vaginal orifice was seen. During the 3rd and 4th weeks there were feeding difficulties which necessitated treatment at the clinic. At the 4th week severe vomiting and loss of weight commenced and persisted until death at the age of 6 weeks. During the terminal illness a paediatrician noted palpable masses in the loins; these at the time were thought to be enlarged kidneys but in view of the postmortem findings may well have been the hypertrophied adrenals.

CASE 2. The 3rd child was born 2 years later and weighed 9 pounds. There was gross hypertrophy of the clitoris and no vaginal orifice was seen. The determination of sex aroused considerable discussion and on the whole opinion favoured the diagnosis of a male. The baby was well until 4 weeks old, when it died in the course of a day from a sudden attack of vomiting.

Postmortem findings. The postmortem appearances of the 2 infants were similar except that in the first there was considerable wasting and the lungs showed early bronchopneumonia.

Externally there was hypertrophy of the clitoris, which was grooved on its under surface, the groove running backwards to the urethral orifice. The general structure was similar to that of hypospadias in the male. The urethra and vagina had a single orifice externally but the two were separated by a septum which reached almost to the vulva; the urethra and vagina were in fact well developed. Normal uterus and ovaries were present. Apart from the adrenals, the internal organs were not abnormal. The adrenals were enlarged and weighed 8 g. each (normal 3–4 g.). The cortex was finely convoluted, producing a great increase in the total cortical tissue.

Microscopically the clitoris contained much erectile tissue. The rudiments of prostatic glands were present at the base of the bladder, and in the urethro-vaginal septum (fig. 2). The uterus and ovaries were normal (fig. 1). The adrenal cortex was markedly increased in thickness and, compared to the normal, there was less regularity in the general arrangement of the cells. There was no abnormally persisting foetal cortex, but the demarcation between cortex and medulla was less sharply defined than usual (figs. 3 and 4). Fat was almost absent from the cortex. Vines' fuchsinophil reaction for the demonstration of androgens was carried out, but the results were not helpful because there was as much fuchsinophil material in the normal control adrenal. However, the reaction is recognised to be unreliable in postmortem material. The pituitary showed an increase in the proportion of basophil cells in the anterior part. These were all normal granular basophils; none of the hyaline basophil cells described by Crooke were found.

Female pseudohermaphroditism is relatively rare; about 100 cases have now been described. The defect is less clearly hereditary than is male pseudohermaphroditism. However, in a number of families more than one member of a generation were involved. The defect has not been traced through several generations. The abnormality was recorded in sisters by Ogston as early as 1872. Hypertrophy of the adrenals was specified by Löser and Israels (1923), Polzer and Priesel (1938), and Young (1937) in their cases (Table I). O'Farrell (1935) described a family in which 2 sisters and a cousin were known to be affected, and 2 children who died in infancy probably had a similar defect. The adrenals were not noted, but later a laparotomy on one of these individuals revealed that these were enlarged (Wilkins *et al.*, 1940). Durlacher (1912) recorded cases which might belong to this category but the adrenals were not mentioned. Rhodes (1943) described the abnormality in twins but again the adrenals were not examined. Two other families were recorded by Apert (1928) and Orel (1929), in which the adrenals are said to have been enlarged, but the original papers are not available.

An exactly similar hypertrophy of the adrenals may occur in the male, leading most commonly to enlargement of the penis, hirsutes, rapid growth, unusual muscular development and premature fusion of the epiphyses (Rolleston, 1936; Priesel, 1931; Cohen, 1946; Jacobzimer and Gorfinkel, 1936; Wilkins *et al.*, 1940). Families are recorded in which a male showed precocious development and a female pseudohermaphroditism (Priesel, 1931, Jacobzimer and Gorfinkel, 1936; Wilkins *et al.*, 1940) (see Table II).

More rarely adrenal hypertrophy in the male may lead to male pseudohermaphroditism and one family is recorded in which both male and female pseudohermaphroditism were associated with adrenal hypertrophy (von Werthemann, 1935: 1941).

The Role of Adrenal Hypertrophy.

The evidence that female pseudohermaphroditism is due primarily to an abnormal secretion of hormones is now very convincing. In certain animals, particularly pigs and cattle, the placental circulation of male and female embryos may

be mingled, and the female becomes a freemartin. The administration of androgens to experimental animals during pregnancy leads to the birth of female pseudohermaphrodite offspring. An interesting case in this connexion was recorded by Brentnall (1945). A woman of 26 with an arrhenoblastoma of the ovary developed virilism during pregnancy and was delivered of a typical female pseudohermaphrodite infant. Where the urine of female pseudohermaphrodites has been examined the excretion of androgens has been found to be above the normal level (Talbot *et al.*, 1942; Fraser, 1945).

A feature of some interest is the occasional coexistence of hypertrophy of the adrenal cortex and interstitial celled tumours of the testis (Wilkins *et al.*, 1940; Cohen, 1946). These tumours alone are well recognized as a cause of precocious development. In some cases a similarity between the tumour cells and those of the adrenal cortex has aroused comment. This association may possibly be connected with an anatomical relationship between the primordia of the adrenal cortex and medullary tissue of the gonad which has been recorded particularly in amphibians (Vannini, 1946).

It has often been suggested that the syndromes which occur with congenital hypertrophy and tumours of the adrenal cortex are similar in the pathogenesis. In both there is an abnormal balance of hormone secretion and a tendency to virilism. It should, however, be noted that in carcinoma of the adrenal cortex there is most commonly some degree of muscular atrophy, osteoporosis, obesity and often insulin resistant diabetes while the androgenital syndrome of congenital hypertrophy of the adrenal cortex is usually associated with precocious muscular and skeletal development and diabetes is rare. This distinction may possibly indicate a preponderance of different hormones in the two conditions (Albright, 1942). In Cushing's syndrome, characteristic of adrenal cortical carcinoma, there may be a relative excess of the hormones involved in the breakdown of tissue proteins to sugar (notably 17 hydroxy- 11 dehydrocorticosterone) while in the androgenital syndrome hormones of the androsterone group may be dominant.

The rare occurrence of male pseudohermaphroditism with congenital hypertrophy of the adrenal cortex (von Werthemann, 1935: 1941) may possibly be due to an excessive secretion of oestrogens by the adrenal cortex. These cases also have their parallel in cases of carcinoma of the adrenal, for although virilism is the commonest sequel, feminism may occasionally occur (Matthias, 1922; Holl, 1930).

Diagnosis and Treatment.

It has already been emphasized that the diagnosis of sex may be very difficult. In Case 1 the sex was correctly determined by the general practitioner because there was loss of blood from the vulva in the first few days of life. This occurrence suggests the presence of a uterus and may prove a useful diagnostic sign. In the first child also palpable masses were present in the loins. It is not known how frequently the hypertrophied adrenals may be palpable but this finding in a pseudohermaphrodite might suggest that the infant was likely to be a female.

Infants with this type of adrenal hypertrophy not infrequently die in early childhood. Of the 38 cases summarized in Tables I and II, 15 died before the age of 6 years, and 9 before 6 months with diarrhoea or vomiting. Dijkhuizen (1943) published a series of 4 cases in which the vomiting was so severe and persistent that a diagnosis of pyloric stenosis was considered. A similar case was also recorded by Skelton (1945). This feature may

TABLE I. *The Familial Incidence of Female Pseudohermaphroditism.*

Author and date	Sex	Age	Clinical features	Adrenals	Notes
Durlacher, 1912	F.	20 months	Hypertrophy of clitoris	?	Children large for their age.
	F.	6 months	Hypertrophy of clitoris	?	Two other children died in infancy.
Apert, 1928	F.	—	Hypertrophy of clitoris	? +	
	F.	—	Hypertrophy of clitoris	? +	
Löser and Israels, 1923.	F.	21 years	Hypertrophy of the clitoris	Demonstrated to be enlarged by X-ray	
	F.	19 years	No separate vaginal opening Male bodily form		
Orel, 1929	F.		Hypertrophy of clitoris	? +	
	F.		Hypertrophy of clitoris	? +	
Rupilius, 1933	F.	1 month	Hypertrophy of the clitoris and no separate vaginal opening	Enlarged adrenals demonstrated at postmortem	Both children died.
	F.	4 months			Four other normal children.
O'Farrell, 1935	F.	24 years	Hypertrophy of clitoris	Enlarged adrenals seen at operation	Eight normal children.
	F.	19 years	Hypertrophy of clitoris	?	
	F.	9 years	Hypertrophy of clitoris	?	Three normal children. Cousins of above.
	F.	Dead	Hypertrophy of clitoris	?	Died in infancy.
	F.	Dead	Hypertrophy of clitoris	?	Nine normal children. Cousins of above.
Young, 1937	F.	16 years	Hypertrophy of clitoris Vaginal opening into urethra Male bodily form and hirsutes	Enlarged adrenals demonstrated by X-ray	
	F.	6 years	Similar		
	F.	3 years	Hypertrophy of clitoris Vaginal opening into urethra	+	Children very large for their age.
	F.	8 months	Similar	?	
	F.	16 years	Clitoris 5 cm. long Vaginal opening into urethra	Enlarged adrenals seen at operation	Partial adrenolectomy with doubtful results.
	F	13½ years	Similar		
Polzer and Priesel, 1937	F.	5 months	Hypertrophy of clitoris No separate vaginal opening Prostatic tissue in the urethrovaginal septum	Enlarged adrenals demonstrated at postmortem	Both infants died with diarrhoea and vomiting.
	F.	1 month			
Rhodes, 1943	F.	At birth	Hypertrophy of clitoris	?	Twins.
	F.	At birth		?	
Biggs and Rose, 1947.	F.	6 weeks	Hypertrophy of clitoris	Enlarged adrenals demonstrated at postmortem	Both infants died with vomiting.
	F.	4 weeks	Hypertrophy of clitoris		

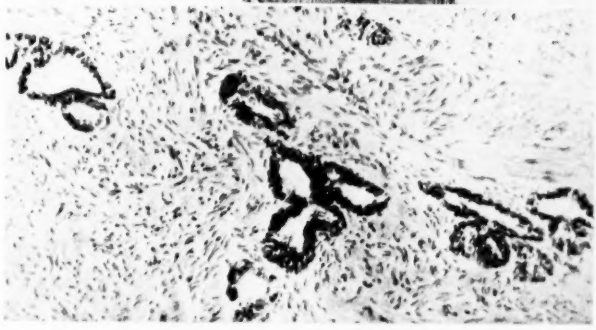

FIG. 1 (above). Low power view of the uterus, bladder and part of the vagina in Case 2.
(R.I. P.M. No. 86/46 × 5)

FIG. 2 (below). Higher magnification of several rudimentary prostatic glands taken from the region marked in Fig. 1.
(R.I. P.M. No. 86/46 × 110)

B. & R.

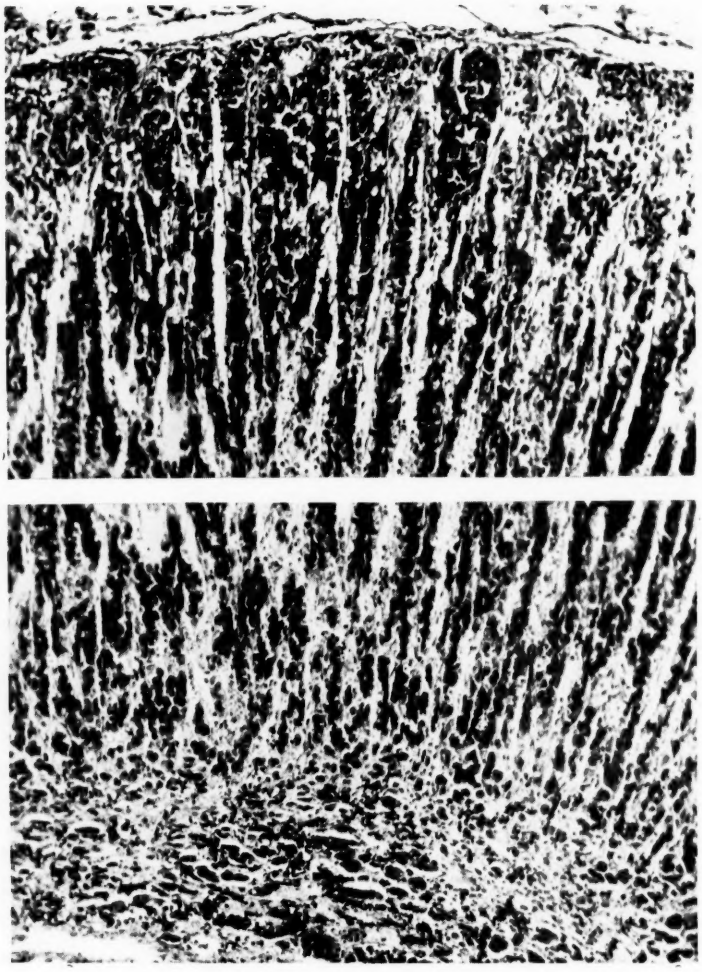

FIG. 3 (above). The outer zone of the adrenal cortex from Case 2. (R.I. P.M. No. 86/46 × 110)

FIG. 4 (below). The inner zone of the adrenal cortex from Case 2. (R.I. P.M. No. 86/46 × 110)

B. & R.

possibly be due to desoxycorticosterone deficiency. This suggestion appears reasonable, not only because diarrhoea and vomiting are common symptoms of desoxycorticosterone deficiency, but also in one or two older patients the mode of death was more definitely indicative of adrenal failure. In 1 of these cases described by von Werthemann (1941) the infant had pigmentation of the skin. In the child of 3 years described by Wilkins *et al.* (1940) death occurred rather suddenly following an indefinite illness associated with pigmentation of the skin, a craving for salt and an elevation of the non-protein nitrogen to 99 mg. per cent. Then the child of 5 years described by Priesel (1931) had pigmentation of the skin and died with a very mild attack of scarlet fever. Again, the young man described by Cohen (1946) died with a profound circulatory collapse out of all proportion to the severity of the pneumonia from which he was suffering. The evidence is at least sufficient to warrant the administration of desoxycorticosterone during an attack of diarrhoea and vomiting, or in infections with a disproportionate circulatory collapse.

With regard to plastic operations for the reconstitution of "normal" external genitalia, the only point which requires emphasis is that no such operation should be undertaken without incontrovertible evidence of the true sex.

The question of adrenalectomy in the female pseudohermaphrodite naturally arises. There are two factors which militate against this treatment. In the first place the pathological effects of excessive androgen excretion would be far advanced when such an operation could safely be undertaken. In the second place the adrenal hypertrophy is usually bilateral and any partial operation would leave the

TABLE II.

The Familial Association of Female Pseudohermaphroditism with Precocious Development in the Male and Male Pseudohermaphroditism.

Author and date	Sex	Age	Abnormality in sexual development	Adrenals	Notes
Priesel, 1931	F.	Infant	Hypertrophy of clitoris	?	Died in infancy.
	M.	5½ years	Precocious development	+	Pigmentation of skin. Died at 5½. Parents related and congenital abnormalities in 2 other children.
Jacobzimer, Gorfinkel, 1936	M.	4¾ years	Precocious development	?	Interstitial celled tumour of testis.
	F.	3 years	Hypertrophy of clitoris	?	
	F.	7 months	Hypertrophy of clitoris	?	
Wilkins, Fleischmann and Howard, 1940	F.	—	Hypertrophy of clitoris	?	
	M.	3 years	Precocious development	+	Died with signs suggesting adrenal failure.
von Werthemann, 1935 and 1941.	M.	8 weeks	Atrophic undescended testes—Hypospadias	23 g.	All died in early infancy and post-mortems were performed.
	F.	12 weeks	Hypertrophy of clitoris	24 g.	
	M.	8 weeks	Descended testes and Hypospadias	24 g.	
	F. Cousin	4 weeks	Hypertrophy of clitoris	15 g.	Cousin marriage.

original imbalance of hormones. Few cases of congenital adrenal hypertrophy have been subjected to operation and, in comparison with adrenalectomy for tumours, the results are not encouraging.

SUMMARY.

(1) Two cases of female pseudohermaphroditism associated with adrenal hypertrophy and occurring in the same family are described.

(2) The primary defect is probably adrenal hypertrophy, for a similar hypertrophy in the male may be associated with precocious bodily and sexual development.

(3) The defect may be familial in that more than one member of a single generation may be involved. Nine families are recorded in which 2 sisters were pseudohermaphrodites, and in 4 families both males and females were affected.

We should like to express our thanks to Dr. A. H. T. Robb-Smith and Professor Chassar Moir for their interest and assistance. We should also like to thank Dr. Skinner, who first saw these children in general practice and whose interest stimulated this investigation.

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A Fatal Case of Primary Diphtheria of the Cervix and Urethra

BY

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AND

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DIPHTHERIA of the female genital tract is seen sufficiently rarely to warrant the recording of the present case. Few of the standard textbooks contain any reference to the subject, and some of these dismiss it in a few lines as being of extreme rarity (Kerr, *et al.*, 1944; Eden and Lockyer, 1935; DeLee and Greenhill, 1943; Stander, 1945; Wharton, 1943). Beacham and Rice (1944) reported that Eigen in 1932 recorded 115 cases, of which only 72 had been confirmed bacteriologically. They collected 13 more cases from the literature, and added 1 of their own. Primary genital diphtheria is rarely diagnosed, but this may be due to the minimal local symptoms and signs. Parks (1941) pointed out that diphtheritic infection of the vagina and cervix is rare in the adult, as the *Corynebacterium diphtheriae* prefers to grow in air and an alkaline medium.

CASE REPORT.

The patient, an unmarried woman, was admitted to a British military hospital in Germany in May 1946. Two days previously she had started an illness of influenza type, with pyrexia of 104°F. The temperature had fallen to 99°F. the day before admission. Her last menstrual period had started 8 days before admission, and had been normal until the onset of her illness, when the loss became muco-purulent and bloodstained. On examination she was found to be tender in both iliac fossae, and a diagnosis of salpingitis was made. Nothing abnormal was found on rectal examination. Treatment was instituted with sulphathiazole 20 g. and hot vaginal douches.

She was first seen by one of us (J. B.) on May 14th, 1946. She complained of some breathlessness and pain in the chest. Nothing abnormal was found in the throat, heart or lungs. The menstrual period appeared to be just finishing. The urethral meatus was red and inflamed, and there was a thin urethral discharge. The cervix was red, with some discharge, but there was no membrane. The pelvic organs were otherwise normal. Specimens were taken for bacteriological examination, with the following results:

Smears:

Urethra. Scanty pus cells. Few gram-positive bacilli.

Cervix. Considerable number of pus cells. Scanty gram-positive cocci and gram-positive bacilli.

Cultures:

Urethra. Gram-positive bacilli.

Cervix. Heavy growth of staphylococci (coagulase-positive), and gram-positive bacilli +++ (?Diphtheroid), later identified as *C. diphtheriae mitis*.

Catheter specimen of urine. Moderate cloud of albumen; white blood corpuscles; epithelial cells; and amorphous urates.

Culture: Staphylococci and gram-positive bacilli.

In view of the unusual bacteriological findings further cultures were examined, with these results.

Urethra. Morphological *C. Diphtheriae*, identified as *mitis* strain.

Cervix. *C. diphtheriae* grown, identified as *mitis* strain. Virulence tests were later found to be positive.

Nose and throat. No *C. diphtheriae.*

On the firm diagnosis of diphtheria, treatment was given with intramuscular anti-diphtheritic serum 96,000 units, and an intramuscular drip of penicillin. Polyneuritis and myocarditis were evidently already present when treatment was started, as examination at this stage showed diminished tendon reflexes, associated with tingling in the tongue and limbs. Nothing abnormal was found in the heart and lungs, but the blood-pressure was 85/65. X-ray of the chest was normal. The inflammation of the urethra had cleared up, but there was a profuse, thin, purulent discharge from the cervix and vagina. After treatment, clearance swabs from the cervix were negative, but the patient's general condition deteriorated. The myocarditis progressed. The heart showed multiple extrasystoles, and there was increasing oedema and oliguria. Moist sounds appeared at the base of the right lung. On June 9th the patient had a vagal block attack, and died the following day, after a further collapse which failed to respond to oxygen and restorative measures. Postmortem examination was not performed.

When the diagnosis of diphtheria had been made the patient was questioned as to possible contacts, and she stated that her bethrothed, a " displaced person ", had been in prison 6 weeks previously, and had shared a cell with a man who had diphtheria. We were later able to take swabs from the bethrothed: *C. diphtheriae mitis* was found in the throat swab. *C. diphtheriae* was not found in urethral swabs. The vast majority of cases of diphtheria in Germany at the present time are due to a virulent *mitis* strain of *C. diphtheriae.*)

Comment.

The route of infection in a primary case of genital diphtheria is a matter for speculation, but it appears possible that it may sometimes be transmitted by sexual intercourse, although we were unable to establish this in the present case. Opinion is divided on the severity of the condition. Whereas Stander (1945) states that the course is usually benign, DeLee and Greenhill (1943) stress the toxaemic effects in spite of the mildness of the local symptoms and signs, and the present case supports this view. There are sufficient numbers of toxic and fatal cases recorded to indicate that the matter is a serious one (Parks, 1941; Cantrell, 1934; Grant, 1934, 1938). The local signs in the present case were not very marked, and it was impossible to make a diagnosis on clinical evidence alone. In diphtheria, bacteriological diagnosis may be made too late for specific treatment to be effective, as was the case here.

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We should like to record our thanks to Colonel P. T. L. Day, O.B.E., R.A.M.C., Officer Commanding the British Military Hospital, for permission to publish this case.

Haematometra caused by disappearance of the Cervical Canal after Labour

BY

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THE following is a report of a case in which the cervical canal was obliterated after labour, and an account of the conservative surgical treatment of the resulting haematometra.

Obstetrical history. The patient, a primipara, aged 27 years, was delivered on June 9th, 1943. Early in May she showed signs of hydramnios, with a sudden increase in the size of the abdomen in early June. Induction by bougies was carried out on account of acute discomfort and dyspnoea.

The membranes ruptured spontaneously and the os dilated fully but, as there was no advance of the head, forceps were applied, and a stillborn male child was delivered. The placenta was retained and was removed manually. There was a small perineal tear which was repaired.

On June 17th the temperature rose and the patient was transferred to Cheltenham Hospital; she was diagnosed as parametritis and later developed a white leg. Early in August she returned home and was able to resume her household duties.

I first saw the patient on March 27th, 1944. She was complaining of amenorrhoea since her confinement, with attacks of pain at monthly intervals.

Examination. On examination the uterus seemed normal. There was an enlarged left ovary. There was also considerable scarring in the vaginal vault and no cervix could be felt or seen.

Examination under an anaesthetic revealed considerable scarring of the vaginal vault, with a small pucker on the right side, which would just admit the point of a fine probe, but this would not enter any distance. The uterus appeared to be slightly enlarged and the left ovary considerably so. I advised the patient that a laparotomy was necessary. She and her husband agreed that this should be done.

Operation. The vagina was packed and the abdomen opened. Fig. 1 illustrates the condition found. The uterus was slightly enlarged, both Fallopian tubes were distended, the abdominal ends being sealed and the left ovary was obscured by a cystic collection of altered blood. The uterus, at its lower end, was separated from the pack-distended vagina by a flat band of fibrous tissue about an inch in length. The cystic collection of blood was removed from the left ovary, the blood was expressed from both Fallopian tubes, and the uterus opened on its anterior surface. It was full of dark menstrual blood, which was cleaned out. A probe was pushed through the scar tissue closing the lower end of the uterine cavity, and cutting down on this, the uterus was laid open along the whole length of its anterior surface. The vagina was then opened transversely (See Fig. 2). The posterior edge of the vaginal opening was stitched to the uterus so that vaginal mucous membrane was in continuity with the endometrium, the stitching being completed around a tube stitched to the fundus of the uterus and passing into the vagina.

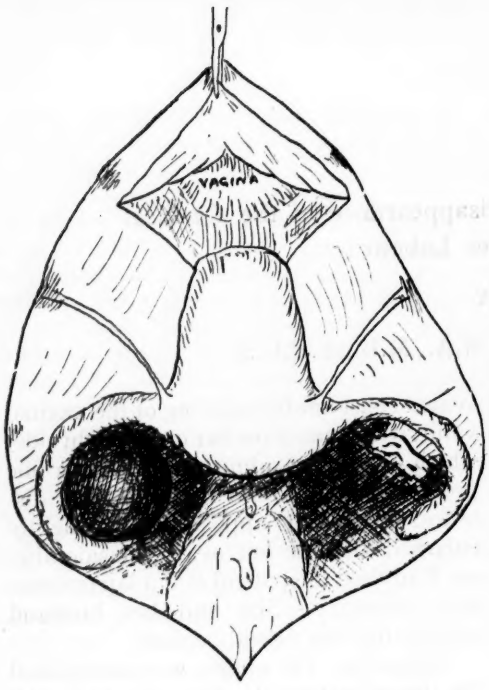

FIG. 1.

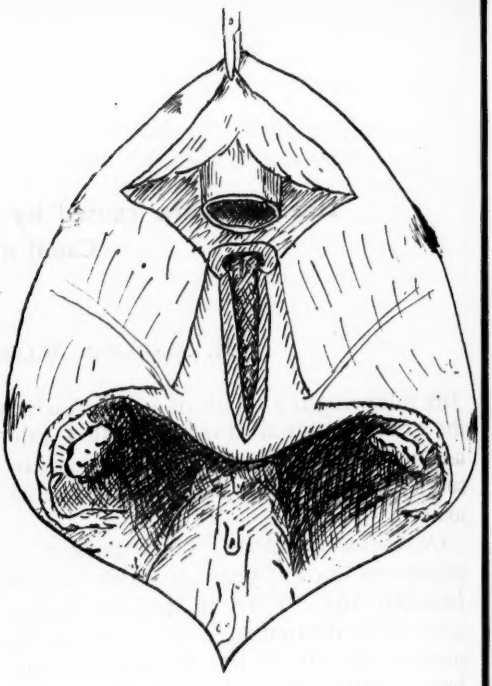

FIG. 2.

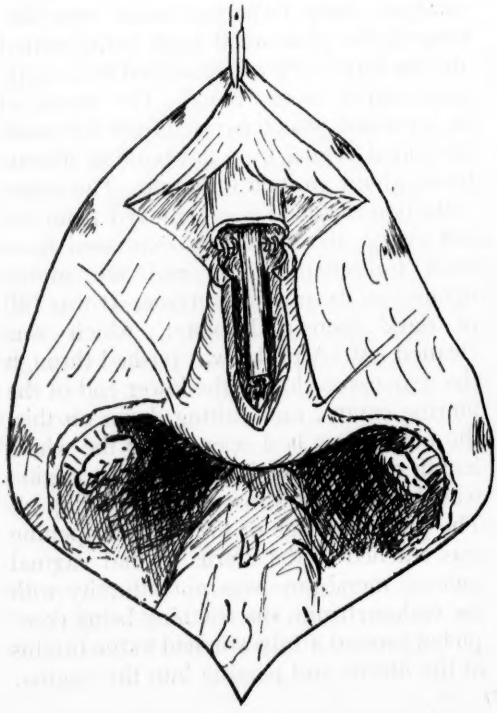

FIG. 3.

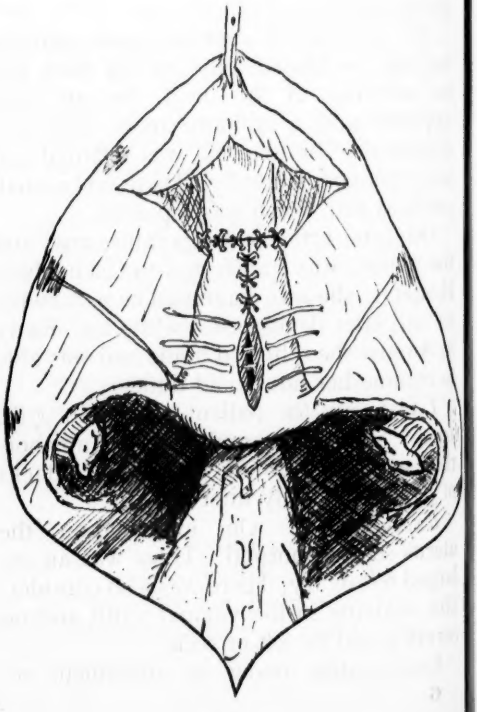

FIG. 4.

Repair of the uterus was then completed (Figs. 3 and 4). The tube remained in for 14 days. Convalescence was apyrexial and uneventful. The patient left hospital in under 3 weeks.

The patient was seen again at intervals during the next 5 months. The first period was accompanied by pain on the first day and lasted 5 days. She was examined at the end of the loss. The menstrual flow was coming through a small opening in the scar in the vaginal vault, which would easily admit a probe. She had regular normal 5-day periods with no pain up to the time she was last seen, 5 months after operation, when the pelvic organs were found to be normal on examination, except for the absence of the cervix. She was advised that there was no reason why she should not embark on a pregnancy.

It is doubtful whether, in the absence of a cervical canal, with its ciliated epithelium, a pregnancy will take place, but she has the knowledge that she is still complete and that pregnancy is not impossible.

This case is one of considerable rarity. In a series of 19 cases of haematometra reported by Berstein and Walker (1939) 2 only could be ascribed to obstetric injuries, while Tait (1945) describes a very similar case for which he removed the uterus.

The reason for this record, apart from the rarity of the condition, is to draw attention to the value of a conservative attitude to the surgery of the female generative organs. Hysterectomy is a fatally easy operation, and it is often not realized how mutilating it is, and that the psychological trauma in nearly all women is considerable, and, in the young, very great.

I was fortunate in that I had personal knowledge of a striking case, exemplifying the conservative attitude, in which functioning double uteri were united and joined to an artificial vagina made at the same time by inlay grafting (Bonney and McIndoe).

My thanks are due to Dr. Scott Kerr of Cheltenham for his note of the obstetrical history.

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Foetal Brain Tumour as a Cause of Dystocia

BY

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TUMOUR of the foetal brain as a cause of dystocia is an exceedingly rare condition, and the writer has found only 1 case recorded in the literature which gives a history of difficult labour presumably due to this cause. This case is described by Russell and Ellis (1933), who are more interested in the histological and pathological studies than in the obstetrical significance. They report the case history as follows:—

"Left cerebral glioma in a stillborn infant. Stillborn at term. The mother was 28 years of age. She had 4 children who were alive and well, and no miscarriages. Pregnancy had been normal except for frequency of micturition during the later months. Strong labour pains began on May 24th, 1925. On the following day instruments were unsuccessfully applied by a private doctor. The mother was then admitted to the London Hospital under Dr. Russell Andrews; an anaesthetic was given at 11.45 a.m. on May 26th, 1925, and a 7 pounds stillborn foetus was delivered without instruments. The foetus was in the right occipito-posterior position when the first examination was made and in the right occipito-anterior position when delivered."

A diligent search of the literature has not brought to light report of any case in which a foetus with an intra-cranial neoplasm has survived labour. Such a case might be recorded as one of tumour growth in infancy. In 1,028 records of conditions diagnosed as brain tumours in the National Hospital, London, Critchley (1925) found only 1 case occurring in infancy, the signs developing after birth. In Cushing's series (1927) there were 1,108 verified tumours of the brain, and of these only 24 were in children under 5 years of age. In no case was there reason to suspect the growth at time of birth. He describes a huge teratoma found in an infant 2 months old supposedly normal at birth (Cushing, 1932). The literature dealing with tumours of the brain in infancy has been reviewed by Gross (1934), and in all of the cases recorded the affected infants were apparently normal at birth, the evidence of tumour growth becoming manifest only some time after. In several of these cases, however, signs developed so early as to suggest that the neoplasm was present during intra-uterine life, their sudden appearance, even a few days after birth, being due to the rapid development of hydrocephaly. Hydrocephaly is stated to be the most prominent feature in most cases, and, as obstruction of the cerebrospinal-fluid circulation may be produced by comparatively small tumours, it is possible that if a search were made for the cause in every case of foetal hydrocephaly, the obstructive nature of the lesion would be demonstrated more often than it is. Cushing describes a group of congenital intracranial tumours, the majority representing suprasellar lesions arising from an anlage of Rathke's pouch. While these tumours seriously interfere with development of the pituitary body there is no record of any such tumour showing its presence in the foetus or in early infancy.

The following is the history of a case of

obstructed labour due to a large tumour of the foetal brain.

The patient, a primigravida, aged 25 years, was admitted to the Rankin Maternity Hospital on February 20th, 1943, as a case of prolonged labour. According to the history she was 38 weeks pregnant and had gone into labour on the morning of February 18th, the membranes having ruptured soon after the onset of pains. She was sent into hospital 60 hours later because of failure of the presenting part to advance and because pains had almost ceased. Many vaginal examinations had been made both by the doctor and the midwife, and she had been encouraged to bear down with her pains. On examination she was found to be a well nourished, healthy-looking woman, but quite exhausted. The size of the abdomen suggested a 36 weeks' pregnancy. Foetal heart sounds were present but the position of the foetus was difficult to determine, and the presentation was queried as a breech. Vaginal examination found an oedematous cervix with a 3 fingers' os. The presenting part was high up and difficult to recognize but again breech was queried. It was not impacted but mobile and above the brim. Pelvic capacity was apparently normal. Uterine contractions being absent and the patient exhausted, she was given morphine and scopolamine. She slept overnight and, on the following morning, labour pains having begun again, she was examined under anaesthesia. It was then established that a very large head was presenting but differing from the typical hydrocephalic head in so far that the impression was received of a solid rather than fluid content. Nevertheless it was thought that this was a case of hydrocephaly with the fluid under considerable tension. The skull was then perforated, and, no bone edges being palpable, the case was left to nature. It was noted at the time of perforation that relatively little cerebrospinal fluid escaped and that the skull had not collapsed to the same extent as it usually does in these cases. As labour progressed, however, a very large quantity of tissue was extruded and gradually piled up in the bed. This tissue was whiter in colour and less friable in texture than normal brain tissue, while its mass explained without doubt the enlargement of the head. A sample of this tissue was sent to the pathologist, who reported as follows:—

"The specimen is of brain tissue compressed by a teratomatous growth comprised of mesodermal and ectodermal elements—cartilage and fibrous stroma and glandular elements presenting appearances similar to (1) ovary, (2) alimentary tract, (3) breast or salivary tissue. The stroma varies considerably from 'adult' fibrous tissue to more cellular undifferentiated tissue."

The foetus weighed 4 pounds 13 ounces, and its length was 19 inches. Reconstitution of the head by packing the cranial cavity with cotton wool showed that the occipito-frontal circumference must have been about 19 inches.

Apart from pyelitis which quickly responded to treatment the puerperium was uneventful.

ACKNOWLEDGMENTS.

I am indebted to Dr. R. H. Heggie for the pathological report, and to Dr. Johnstone, Medical Officer of Health, Greenock, through whose courtesy this case is published.

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A Case of Serous Adenofibroma of the Ovary

BY

A. SHARMAN, M.D., M.R.C.O.G.

AND

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SEROUS adenofibroma is one of the rarest of all ovarian tumours. Indeed a careful study of the British literature failed to reveal a single case-report. The subject of serous adenofibroma and cystadenofibroma of the ovary has, however, been discussed in some detail by Scott of Baltimore. He stresses the great infrequency of such cases in the literature, which he sums up as being extremely scant and often questionable because of incomplete descriptions and more recent conceptions of various tumour types. In spite of this, he is of the opinion that they constitute a definite subgroup of serous epithelial tumours of the ovary.

In his review Scott states that in the case reports of ovarian tumours in the files of the Johns Hopkins Hospital, extending over 20 years and embracing a total of 26,000 gynaecological cases, 13 reports of such tumours were discovered and 1 report was found in the general pathology files. Many of these specimens came from other hospitals, some in Baltimore and some in other cities. A number of the tumours, particularly the earlier ones, were filed under other diagnoses.

The clinical features of the 14 cases are summarized and the pathological features are discussed in detail. Scott divides tumours of this type into 2 groups, serous adenofibromas, which are principally solid, and cystadenofibromas, in which some areas are solid and others show large cysts. In his series there were 8 adenofibromas and 8 cystadenofibromas, bilateral tumours being found in 2 patients.

CASE REPORT.

The principal features of the present case are as follows. The patient was aged 56 years and complained of vaginal bleeding of 2 months duration, commencing 11 years after the menopause. She had been married 33 years and had had 2 normal pregnancies. On examination a large, firm, abdominal tumour was found rising out of the pelvis to about the level of the umbilicus, a provisional pre-operative diagnosis of fibromyoma being made.

On March 29th, 1946, one of us (A.S) opened the abdomen, when the mass was found to be a solid tumour of the left ovary. The uterus and right Fallopian tube and ovary appeared normal. A small amount of free fluid was present in the peritoneal cavity. Left ovariotomy and resection of a portion of the right ovary were performed, the uterus being conserved. The patient made a satisfactory recovery and was dismissed well on the 22nd day after operation.

The ovarian tumour was firm, compact and lobulated, measuring 7 inches by 5 inches by 4½ inches. On section a few small cystic spaces were seen but the bulk of the tumour was solid. The attached Fallopian tube was elongated but showed no other abnormality. On microscopic examination 2 constituent elements were found, namely a fibromatous stroma and a large number of gland-like or cystic spaces of varying

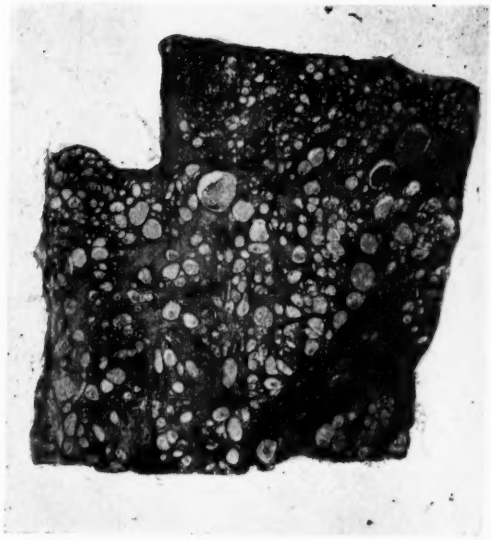

FIG. 1.

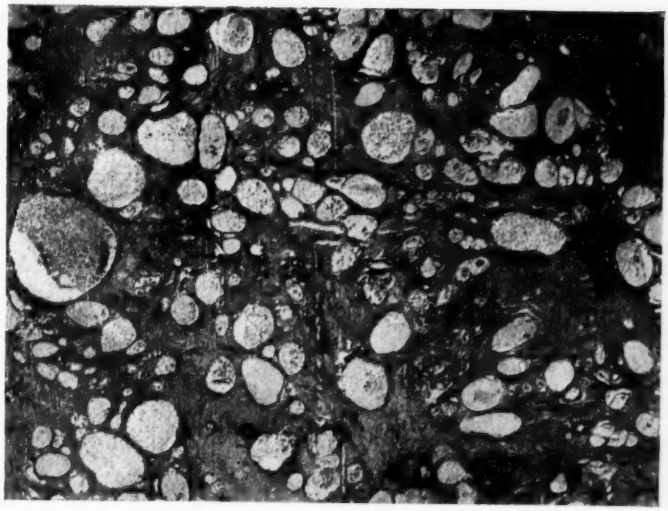

FIG. 2.

S. & S.

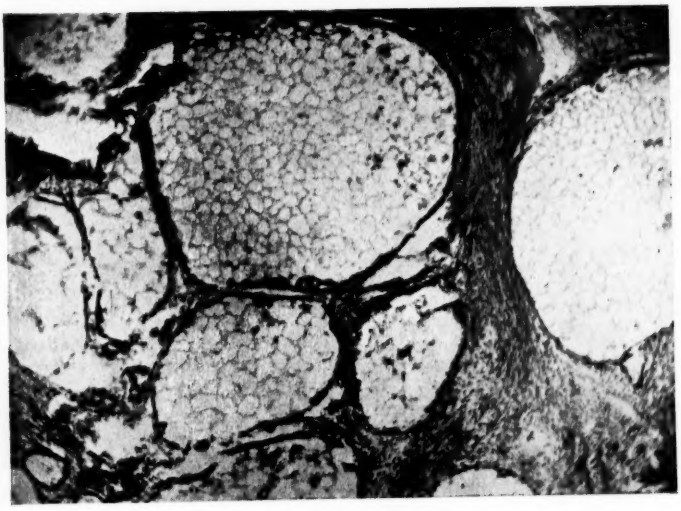

FIG. 3.

size. The stroma was exactly the same as that of an ordinary fibroma of the ovary, with narrow strands of fibrous tissue running in all directions. The adenomatous areas were usually circular or oval but occasionally had an elongated or irregular outline. In some places tiny papillary projections into the cyst spaces were seen. The spaces were lined by columnar, cubical or flattened epithelium, which was compactly arranged, usually in a single layer, with centrally-placed nuclei. No evidence of malignancy was found. The histological features are seen in Figs. 1, 2 and 3.

The patient reported 10 months after operation. Since dismissal she had remained well, there being no recurrence of the vaginal bleeding. On vaginal examination the cervix and body of the uterus were found to be atrophic.

Thanks are due to Dr. Emil Novak for his kindness in giving us his opinion on the original sections from this case. Thanks are also due to Dr. Donald McIntyre, into whose wards this patient was admitted.

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ROYAL BELGIAN SOCIETY OF OBSTETRICS AND GYNAECOLOGY

In accordance with the wishes of the Committee of Management of the former International Congress of Gynaecology and Obstetrics, the Administrative Council and Consultative Committee of the Royal Belgian Society of Gynaecology and Obstetrics, now legal managers of these funds, have decided to utilize the revenues of the Foundation for a prize to the value of 20,000 Belgian francs to be awarded on July 1st, 1949. The prize will be awarded for the best work on Gynaecology and Obstetrics, either in manuscript or published during the 4 years, July 1944 to July 1948.

The works presented should not have already been awarded a prize and should be written in one of the official languages of the International Congress, i.e., English, French, Spanish, Russian, Italian, or German, or translated from one of these languages.

Two copies of the paper should be sent to the Secretary of the Royal Belgian Society of Gynaecology and Obstetrics 12 months before the date fixed for the award of the prize, that is, before July 1st, 1948 (Dr. P. Lavand'homme, 84 av. Paul Deschanel, Brussels).

The examining committee will be chosen by the Royal Belgian Society of Gynaecology and Obstetrics from among its members, honorary members and corresponding members, Belgian or foreign, and according to a method to be ultimately decided by the Society. The president of the Society will be the Chairman of the Committee. Members of the Committee will not be able to take part in the competition.

The decision will be made by a majority vote, and if the Committee decides that none of the submitted works is worthy of the prize, no award will be made and the amount will be added to the value of the next prize.

The prize of the International Foundation of Gynaecology and Obstetrics will be awarded for the second time in July 1949, at the monthly meeting of the Royal Belgian Society of Gynaecology and Obstetrics.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The following candidates have satisfied the examiners for the Diploma in Obstetrics examination. March 1947.

James Rollo Ballantyne.
Alex Carl Barthels.
Douglas Charles Aitchison Bevis.
Geoffrey Ronald Bourne.
Kathleen Anne Clark Bowen.
John Anthony Bowen-Jones.
Leonard Boyars.
Elizabeth Christian May Brunyate.
Joyce Beryl Burke.
Hubert Cedric Burnell.
John Peter Bush.
Wilfrid Ernest Chapman.
Francis James Cockersole.
Denis Pelles Cocks.
Edward Cope.
George Henry Reginald Curnock.
Alice Davies.
Margret Eley Davies.
James Edwin Drabble.
Patricia Mary Elliott.
Geraldine Winn Everett.
Sebastian Carl Jacques Falkman.
Melville Robert Fell.
Harry Johnson Fisher.
Benjamin John Frankenberg.
Jean Margery Frazer.
George Barton Gibson.
Leslie Stuart Glass.
Cornelius Jeremiah Griffin.
Geoffrey Norman Grose.
Elizabeth Mary Harper.
David Hay.
John Anthony Henderson.
George Sigerson Hopkins.
Jean Anderson Horne.
Brian Gordon Isaacs.
Alun Gareth Jones.
Gordon Davidson Kelly.
Janet Farquhar Kennedy.
Norman Armstrong King.
Donald Victor Latham.
Christopher Lewthwaite.
George Ian Louisson.
Carmichael Mackie.
Archibald Torquil McNeil.
Betty Emma Anna Magill.
David Mander.
Edith Marion Metcalfe.
Reginald Thomas Michael.
Charles Ernest Miller.
Albert Milton.
Doreen Mitchell.
Annapurna Mukherji.
Mathew Robert Neely.
George Frank Newbold.
Dennis Nixon.
Helen Margaret Noble.
Margaret Bonney Noble.
Barbara Dorothy Oakley.
Alfred Denis Parsons.
Stanley Dreland Perchard.
Francis Charles Ralph Picton.
Edward Dennis Pond.
Kenneth Ivor Price.
Sidney Wilson Price.
Margaret Randell.
Edwin Noel Rees.
Rachel Richards.
Leslie Frisby Richards.
Joseph Germain Rountree.
William Sword Russell.
Ruth Sabel.
Timothy John Scannell.
Charlotte Sommer-Hirsch.
Kathleen Heyland Stewart.
Bahman Sohrabji Surti.
Cecil Wallis Sweetnam.
Sheila Royse Tangye.
Mary Elizabeth Tighe.
St. John Michael Alexander Tolhurst.
Eric Frank Twiss.
Michael Joseph Twomey.
William Alexander Walker.
Winifred Isobel Watson.
Constance Margaret Watt.
Cecil Trevor Hamilton Whiteside.
Roberta Williams.
John Kendal Wilson.
Sau Haan Wong.
Elizabeth Younger.

BOOK REVIEWS

" A Textbook of Midwifery." By WILFRED SHAW, M.D., F.R.C.S., F.R.C.O.G. Second edition. J. & A. Churchill, London, 1947. Pp. 649. Price 21*s*.

THIS textbook is written for the medical student and is likely to appeal to him. It is of suitable size to be carried about and read while he is travelling; yet it is a serious textbook and no mere pocket book. The print is clear, of suitable size and attractive appearance. Illustrations are profuse, of high standard and each makes clear the point which the author wishes his reader to grasp.

The field of obstetrics is adequately covered for a reader who is preparing himself for a qualifying examination in midwifery—especially if used in conjunction with clinical teaching. Fundamentals are presented clearly. The author tries not only to convey factual knowledge, but also to stimulate the reader to think for himself. When, on a particular subject, divergent authoritative views exist the author says so, and endeavours to present fairly to the reader views with which he personally disagrees. He would rather efface himself and his own views than allow his students to become mere sponges, which when squeezed, would give back what they had absorbed. He understands the student mind and so is able to expose and correct many of its misconceptions.

The book opens with an introduction which the student should read as frequently as any other part of the book. It will encourage him to take a broad view of the subject which he is studying in detail.

In a book of high standard it is difficult to pick out portions for special mention. But the haemorrhages, contracted pelvis, abnormalities of uterine action and the pathology of puerperal sepsis read very well.

It is disturbing, however, to find in a book written principally for undergraduates, that forceps delivery before full dilatation of the cervix is not only condoned but even advocated. What Mr. Shaw does himself in this matter is of little consequence. The expert's judgment and skill are such that he can at times afford to defy certain commonly accepted rules. But is it wise to teach this to the unqualified? Will some unfortunate young doctor, having failed with forceps, return home bitterly to re-read these passages to find out how he misinterpreted them? Will quoting Shaw help the hapless candidate who has incurred the examiner's displeasure at the final examination? Is not the newly-qualified doctor better to lose an occasional baby than to subject the mother to the fearful risk of his applying forceps before the cervix is fully dilated?

Recent work on the rhesus factor and erythroblastosis is adequately summarised. The place of penicillin in the treatment of puerperal sepsis is sketchy. It is unusual to find the original red prontosil (sulphonamide crysoidin) preferred to the sulpha drugs now in common use. The advocated technique of swab taking from the cervix for bacteriological diagnosis in puerperal fever is rather elaborate. The busy doctor will not do it. A simpler technique for the taking of a high *vaginal* (rather than cervical) swab would be more acceptable to him, easier to do and less likely to be omitted altogether.

In spite of these criticisms the book should prove popular and can be recommended with confidence.

" Laparotomia Estetica en la Mujer " (Aesthetic Laparotomy). By Dr. CARLOS LORCA. Pp. 66; 70 illustrations. Madrid: Editorial Cientifico Medica, 1946.

THIS gracefully written and produced monograph is dedicated, in the author's words, to the prevention of the mental distress caused by mutilating abdominal scars in women of whatever age who have to undergo gynaecological operations. Its plea for a nicer planning of laparotomy incisions in women deserves the widest attention. The author shows that the incision he describes gives ample access to the abdominal cavity for most forms of conservative gynaecological surgery and

for Caesarean section and the reviewer confirms his claims after considerable trial of his method. The appendix, too, is easily approached thus and it must be the hope of all of us that we might less often have to see the abdomen of a woman disfigured by those most unsightly of scars, the paramedian and the McBurney, which mark the trail of the appendisectomist.

The author traces precisely on the abdominal skin a transverse incision of not more than 10 cm. in length, within the pubic hair-line, slightly curved, with its centre about 4 cm. above the pubis. He assures its position and symmetry by placing on the abdominal wall a plate of thin metal hooked at either end to fit over the pubis and the umbilicus. The incision is traced with methylene blue through a linear perforation in the plate and symmetrical surture lines are traced through cross perforations. The skin is incised along this tracing. The aponeurosis can be incised at a slightly higher level giving an opening of up to 12 cm. long, and if further space be needed the lower flap is divided longitudinally and then dissected off the underlying muscle. The recti are separated and the peritoneum incised longitudinally. The author advises deliberation and careful haemostasis at all stages, allowing himself 15 minutes to complete the incision and introduce packs and retractors.

The reviewer commends the author's ideals and their mode of presentation in this book. The reader ignorant of Spanish will easily follow the argument from the excellent illustrations alone.

"Gestation Periods. A Table and Bibliography." Second edition. Compiled by J. H. KENNETH, M.A., Ph.D., F.R.S.E. Imperial Bureau of Animal Breeding and Genetics. Edinburgh, 1947. Pp. 30; price 3*s*.

THIS pamphlet provides, in tabular form, details of the lengths of the gestation periods of mammals—average, minimum and maximum. Each item has its reference to the literature. Altogether there are 442 such references. The second edition includes details of 35 additional species and 100 additional references. The pamphlet supplies a complete and ready source of reference to all concerned with the study of comparative reproductive biology.

"A Short Textbook of Midwifery." By G. F. Gibberd. (1947). J. & A. Churchill, London. Price 21*s*.

MR. GIBBERD'S "Short Textbook of Midwifery" extends to 545 pages of letterpress. The arrangement of the contents is planned to present initially a complete picture of normal pregnancy and labour, including a discussion of occipito-posterior position and plural pregnancy, after which abnormalities of pregnancy are discussed, followed by separate consideration of mal-presentations, contracted pelvis, and faults in the forces of labour. Antepartum haemorrhage and abnormalities of the third stage next receive attention, and the book is then concluded by sections on the normal and abnormal puerperium, on obstetric operations, and on neo-natal paediatrics. The difficulties inherent in presenting the subject in this form have been tackled with skill. The book as a whole is readable and its continuity is well maintained.

Certain subjects receive a disproportionately thorough treatment in what purports to be a short textbook. For example the chapter on "Puerperal Infections" extends to 46 pages. This particular chapter, besides being the longest, is probably the ablest and most interesting in the whole book; but the detail in which the subject is considered is more worthy of a place in a highly specialized textbook than in one which is probably designed to meet the needs of the undergraduate and general medical practitioner.

Reading a textbook by this author one instinctively turns to the section on "Toxaemias of Pregnancy", where, however, a disappointment awaits, for, in discussing the nomenclature for the common late toxaemia of pregnancy, Mr. Gibberd decides that the term "Albuminuria of Pregnancy" is preferable to its synonyms, of which he lists "Pregnancy kidney, pre-eclamptic toxaemia, hypertensive toxaemia, and late toxaemia" It is regrettable that Mr. Gibberd should give his authority to the perpetuation of this unsatisfactory term. Furthermore, references to the common occurrence of a chronic nephritis as a sequel to pregnancy toxaemia might justifiably be dropped from a modern textbook. The discussion of the theories of aetiology of eclampsia is an admirable piece of verbal compression, but suffers somewhat from the absence of clearly-headed sub-paragraphs,

while reference to the possible influence of dietetic deficiencies is somewhat perfunctory.

In some general subjects it is good to see the emphasis placed upon the theories of unequal foetal flexibility in relation to internal rotation of the head; and the lucid summary of the uses of X-ray pelvimetry is useful. It is to be regretted, however, that there are so few illustrations to certain sections dealing with manual procedures. In a students' textbook, it is a bold but perhaps justifiable step to avoid illustrations of Caesarean Section (as Mr. Gibberd does), but to find that breech delivery is described in detail entirely without illustrations is very surprising. Such an omission puts a very unfair strain both on the concentration of the student and upon Mr. Gibberd's descriptive powers, outstandingly clear though these are.

The author makes use of a number of statistics in respect of the "Class A" patients at Guy's Hospital, hoping thereby to present figures for the incidence of various complications in an average and unselected population. This is an extremely valuable teaching expedient, which one would like to see emulated in other authoritative writings, in which the statistics are too often unfairly loaded by the use of hospital figures. There are one or two omissions from his statistical survey, however. One would like, for example, to have a clear guidance given to the student of the actual incidence of forceps delivery in the Class A patients, while it might be useful to record the frequency of primary uterine inertia.

Mr. Gibberd's prose style is incisive and lucid. The pedant's ear, however, will be shocked by the very infrequent lapse, e.g., the use of inapplicable adverbs, as in the statement that "excessive vomiting . . . is practically never fatal." It must also be confessed that one such pedant objects strongly to Mr. Gibberd's use of "Syncitium" as an alternative to "Syncytium".

A review of a previous edition of Mr. Gibberd's textbook in this journal summed it up as an essentially "safe" textbook. With this the present reviewer would like to concur, adding that it is also well written, thoughtful, and interesting. Its value would be considerably enhanced by the inclusion of a very short bibliography at the end of each chapter, referring the earnest student to the original publications of the authors mentioned by name in the general body of the letterpress.

W. I. C. MORRIS

REVIEWS OF HOSPITAL REPORTS

MEDICAL AND CLINICAL REPORT OF THE SIMPSON MEMORIAL PAVILION, ROYAL INFIRMARY, EDINBURGH, FOR THE YEAR 1945.

THE report is presented in two parts—obstetric and paediatric. The obstetric section is devoted mainly to patients confined in the hospital, but there is a short summary of 657 district cases of which 13 were abortions. There was 1 fatal case in the district (0.15 per cent maternal mortality). This patient (aged 37, para. 3) had been treated for general debility during pregnancy with iron tonics. At term labour was uneventful but during the 30-minute third stage there was a mild degree of haemorrhage. One hour after delivery she collapsed, but improved with blood transfusion and sedatives. Twenty-four hours later she complained of sudden pain in the left side of the chest, collapsed and died. There was no autopsy. Death is ascribed to acute heart failure. In the absence of a history of heart disease the reader might, perhaps, think the third stage haemorrhage a contributory, if not the principal factor.

In-patients numbered 3,873 among whom there were 3,202 deliveries. This figure includes 49 patients who were admitted after delivery outside. There were 11 maternal deaths. Pyrexia occurred in 58 cases. The standard of morbidity is all fatal cases and all cases in which the temperature reaches 100.4°F. in any 2 of the bi-daily readings from the end of the first day until discharge from hospital or the end of the 21st day after delivery. The morbidity-rate was 2.2 per cent.

Numerical tables show briefly the essential particulars of the important complications of pregnancy and labour encountered and of the obstetrical operations performed. Then follow 3 pages of notes summarizing each maternal death. A comparative table shows the maternal mortality rates for all deliveries, Caesarean section, eclampsia and placenta praevia, the morbidity-rate of all deliveries, the interference-rate—forceps and Caesarean section, and the foetal mortality-rate in uncomplicated primigravid breech delivery for the years 1932–1945.

Single case data are given for contracted pelvis, eclampsia, multiple pregnancy, placenta praevia, cardiac disease, uncomplicated breech deliveries, and embryotomy.

Placenta praevia was encountered in 40 patients who gave birth to 41 babies. There was no maternal death. Of these 41 babies 12 appear to have been stillborn or died (not 13 as stated). Using this apparently erronous figure of 13 it is reduced to 4 on the grounds that 9 were under 36 weeks' maturity. The significant foetal survival-rate is thus claimed to be 87 per cent. (Actually by this means as only 12 babies do appear—from study of single case data—to have died the significant foetal survival-rate could be claimed as 90.6 per cent.) But the only reason for the elimination of these 9 premature babies is that they were dead. Seven other identical premature babies which lived are not excluded. The resulting figure is rather meaningless. It is the survival-rate of all babies of 36 weeks' maturity and over, and of those under 36 weeks' maturity which did not die, born to mothers who had placenta praevia. It would be reasonable to exclude babies who had a congenital deformity incompatible with life. There do not appear to have been any such babies. The foetal survival-rate in this whole series of placenta praevia cases is 70.8 per cent.

The foetal mortality in uncomplicated primigravid breech delivery is given as 10 per cent in a series of 50 cases. The reviewer would personally have eliminated 3 cases where the mother had toxaemia (in 2 the foetus survived and in 1 was stillborn); the corrected foetal mortality-rate would then be 8.5 per cent.

In 51 cases there was either retained placenta, adherent placenta or post-partum haemorrhage. Two patients died. Blood transfusion was given in 33 cases. The forceps delivery-rate was 11.6 per cent and the Caesarean section-rate 5.5 per cent—the maternal mortality-rate of 159 Caesarean sections was 1.98 per cent.

Maternal death occurred in 3 booked and 8 non-booked cases. Postpartum haemorrhage was the primary cause in 2 of the booked cases. In the first details given of the haemorrhage and its treatment are scanty. In the second forceps delivery under chloroform of the after-coming head in an assisted breech delivery was followed by a third stage haemorrhage and collapse. Blood transfusion was given: 2 days later she developed anuria which did not respond to intravenous infusions. She died in coma 6 days after delivery. Rh grouping is not mentioned. The third booked fatal case had toxaemia. She was delivered by Caesarean section under cyclopropane. Her condition was good throughout, but collapse occurred at the end of the operation. She died in spite of transfusion 3½ hours later. The amount of haemorrhage is not stated. Of the 8 emergency fatal cases toxaemia in a wide sense was the underlying cause. At least 7 would appear to have been unavoidable deaths as far as the hospital was concerned. Sepsis, as a major cause of maternal death, can now be controlled. Death from haemorrhage should be largely controllable. But here again as in report of hospital after hospital is the baffling toxaemia problem.

The paediatric section deals with the babies born during the year. The total was 2,730 live births and 132 stillbirths. There were 16 previable (under 2¾ pounds) infants—none survived. The neonatal death-rate was 30.8 per 1,000 live births for all infants (viable prematures 229.4, and mature infants 12.4 per 1,000 live births). At the end of 2 weeks or on discharge 78.1 per cent infants were wholly breast fed. 9.8 per cent infants displayed a morbid course. The causes of morbidity are tabulated. The cause of death was known in 88 out of 89 cases and was determined by postmortem in 71. The stillbirth-rate for all infants was 46.1 per 1,000 live births. The combined stillbirth and neonatal death-rate is 76.9 per 1,000 live births.

THE MEDICAL REPORT OF THE ROYAL SAMARITAN HOSPITAL FOR WOMEN, GLASGOW, FOR THE YEAR 1945.

THERE were 3,700 (corrected for readmissions) patients admitted to this gynaecological hospital. On them were performed 3,468 operations with a mortality of 0.70 per cent.

The bulk of the report consists of a table occupying 20 pages dealing with the pathological conditions encountered. These are tabulated on a regional basis, a general basis including errors of development, conditions resulting from infection, injuries, fistulae and displacements, diseases outwith the genito-urinary tract, and certain non-classifiable conditions. The number of cases is given and with this are correlated certain other facts such as the average age, parity, number married, etc.

A brief summary is given of 26 fatal cases. Nine of these deaths resulted from operations for genital prolapse: 3 are ascribed to shock, 2 to widespread sepsis, 1 to pulmonary embolism, 1 to heart failure 14 days after operation, 1 to acute pyelonephritis while 1 (a diabetic) died in diabetic coma 24 days after operation. It is not possible to calculate the mortality-rate for these plastic operations as the number done is not stated. The number of major vaginal operations performed is given as 486. One abdominal operation and 1 major vaginal operation were performed on the same patient. If we assume that an operation for genital prolapse is a major vaginal operation, and that every major vaginal operation performed in the hospital during the year 1945 was for genital prolapse then the hospital's mortality for prolapse operations is 1.84 per cent. There were 2 anaesthetic deaths: 1 further patient died without regaining consciousness from the anaesthetic after a diagnostic curettage—autopsy revealed chorion-epithelioma with distant metastasis. Four deaths were associated with malignant disease and 1 with congenital heart failure.

A brief description is given of the modified Paris technique employed in the treatment of cervical uterine cancer. Details are given too of the patients receiving deep X-ray therapy, for both benign and malignant conditions, since 1938 with follow-up figures. These figures will be of interest to those who study the results of malignant disease of the female genital organs.

OBSTETRICAL AND GYNAECOLOGICAL REPORT OF THE ROYAL VICTORIA HOSPITAL, MONTREAL, CANADA.

This is a combined report for the 2 years ended December 31st, 1944 and 1945. The total number of beds in the obstetric and gynaecological departments is not stated but the number of patients cared for during these 2 years is large. There were 9,387 adults and 4,759 children—a total of 14,146 patients.

In the obstetric department there were 5,461 in-patients of whom 5,288 were booked and 173 emergency cases. The total number of confinements in the hospital was 4,869 of which some 24, occurring before the 28th week, were abortions. Single case data are given only for adults and infants transferred to other departments, and for maternal deaths. The rest of the report is numerical.

Maternal death did not occur in any case of Caesarean section which was performed on 219 occasions although there was a foetal mortality of 26 (11.8 per cent). Spinal anaesthesia was employed in 203 cases and local in 16 cases. Quite apart from the question of the anaesthetic agent the maternal result is most satisfactory. Doubtless both the protagonists and antagonists of spinal anaesthesia for Caesarean section will be interested in these figures.

The section dealing with infant mortality is perplexing. The deaths are divided into " full-term " (which is an understandable term) and " premature (28 weeks)" (which is not as thus defined an understandable term). In both of these classes a distinction is drawn between " born dead (antepartum, and intrapartum)", " stillborn ", and " died postpartum." Careful study of this table fails to reveal any undefined subtle difference between stillborn and born dead. Undefined, such a distinction is confusing and of no value. It should be eliminated.

The standard of obstetrical morbidity used is a single rise in temperature to 100.6°F. (after the first 24 hours and until discharge). The morbidity-rate, the lowest in the hospital's history, was 16.8 per cent.

The maternal mortality-rate, 0.08 per cent, is the result of 5 deaths. In 3 eclampsia or toxaemia was the cause of death—they were emergency admissions, in terminal condition, and had had no antenatal care at all. In 1 death was due to post-partum haemorrhage 2 hours after a low forceps delivery: labour had lasted 72 hours. Manual removal of the placenta at the time of delivery might possibly have prevented this death. The fifth death was due to ruptured uterus, retro-peritoneal and intraperitoneal haemorrhage in a case of breech presentation with hydrocephalus in which craniotomy was employed.

A special toxaemia clinic, by which all toxaemic patients on the public services were treated, is considered to have justified itself. Educational classes in personal hygiene, food requirements and infant care held in the out-patient department speak for the progressive direction of the obstetrical department.

In the gynaecological department there were 3,926 admissions. There were 7,640 out-patient attendances of which 1,881 were new visits. A broad classification with numerical incidence of non-malignant diseases is given. (Malignant disease is dealt with in the Radium Clinic Report.) The list of operations performed presents no unusual feature. Local colour is given by the performance of Dr. Chipman's operation 348 times out of 450 operations for the cure of sacro-pubic hernia.

Of 27 deaths 16 were associated with malignancy. Of 11 deaths from non-malignant conditions 2 were due to blood transfusion, 3 to pulmonary embolism of which 2 occurred in women under 40 on whom plastic repair for prolapse had been performed, while 1 succumbed to air embolism during tubal insufflation for sterility.

The report closes with that of the Radium Clinic. This includes an excellent summary of the results of cervical and corporeal uterine cancer treated by radium for the years 1926 to 1945.

MEDICAL AND CLINICAL REPORT OF THE WOMEN'S HOSPITAL, CROWN STREET, SYDNEY,

From 1st July, 1944, to 30th June, 1945.

THIS report deals with the patients in the public wards of the hospital. The in-patients are accommodated in one of three departments. These are the Indoor Maternity, the Founders' Block (Isola-

tion) and the Gynaecological departments. In these there were 4,326, 924 and 410 patients respectively during the year. Confinements in hospital numbered 3,616, and on the district 49. The out-patient attendances were large—36,796 adults and 1,056 babies.

In the maternity department there were 3 deaths among booked patients and 6 among emergency cases, making a total of 9 deaths. In the first booked case death was ascribed to acute hepatic necrosis: labour was induced for toxaemia, delivery was instrumental: death occurred 2 days later. The second died of pulmonary embolism following hysterotomy and sterilization for hypertension (250/140) and albuminuria in a pregnancy of 24 weeks' duration. The third death was primarily due to postpartum haemorrhage: a 6-gravida, aged 29, was delivered of a 7½ pounds infant after a normal labour of 1½ hours; a 10-minute third stage was followed by a profuse haemorrhage which was controlled to slight bleeding "and exploration of cervix with speculum showed this to be coming from above os. Blood transfusion continued but, as some bleeding continued, manual exploration of uterus and *laparotomy performed* [reviewer's italics]. As bleeding was still free 2½ hours later, uterus and vagina were packed with gauze. This was removed 36 hours later and patient's condition was satisfactory. She died suddenly from pulmonary embolism on the sixth day of puerperium." It is to be regretted that details of a case so interesting, and probably most instructive, are incomplete. Why the laparotomy? What was found? What was done? In 3 of the deaths among emergency cases toxaemia (2 with eclampsia) appears to be the prime cause. Of the 3 remaining, 1 died of acute appendicitis with general peritonitis; 1 (aged 18) of acute hepatic necrosis and uterine infection following prolonged labour, failed forceps outside and difficult delivery in hospital. The last (primigravida of 24), admitted in poor condition with an impacted breech and history of outside interference, was delivered with difficulty by blunt hook and perforation of aftercoming head. "*Later* [reviewer's italics] manual removal of placenta. Patient was very shocked and died about 14 hours later." What was the length of the third stage? How much haemorrhage accompanied it? Was an additional anaesthetic given for the manual removal? We all meet these difficult cases. Would that the published reports gave full details!

The tables of single case data of complications deserve study. There were 29 cases of placenta praevia. No mother died. But the foetal mortality was 72.4 per cent. On 8 occasions central placenta praevia was treated by version and bringing down of a leg: on each occasion the baby was stillborn.

Caesarean section was performed on 5 occasions but only 2 of the babies survived. Postpartum haemorrhage occurred 241 times (6.6 per cent). Forceps was used 414 times (11 per cent). Caesarean section was performed 34 times (0.9 per cent) without any maternal fatality. The morbidity-rate for the whole obsteric department was 5.6 per cent. This figure cannot be regarded as reliable. The standard of morbidity is said to be that of the British Ministry of Health namely "a temperature of 100.4°F. in the first days of the puerperium, sustained for 24 hours or recurring during that period." It will be observed that this is not the British Ministry of Health standard but a paraphrased version of it, even more ambiguous than the much maligned standard itself.

Stillbirths numbered 124 (27 macerated) which is 33.9 per 1,000 births. If premature and non-viable infants are excluded the corrected rate is 22 per 1,000 births at term. Neonatal deaths numbered 102, i.e., 28 per 1,000 live births; excluding premature and non-viable infants the corrected rate would be 11 per 1,000 live births. The combined stillbirths and neonatal deaths numbered 226, i.e., 61.9 per 1,000 births. This figure can be corrected as the two former to 29.8 per 1,000 births.

Of 283 premature (5½ pounds or less) babies born alive 65 (23 per cent) died. Each stillbirth and neonatal death is set out singly. Autopsy was performed on 102 infants.

From the Founders' Block—Isolation wards and "E" wards—924 or 925 patients were discharged. Of these 835 suffered from some variety of abortion. Patients admitted over 28 weeks pregnant or after delivery of a "viable" infant are not included in these figures, but are dealt with in the Indoor Maternity Report. Among the 900-odd patients there were 5 deaths. Three died of post-abortional sepsis—one due to Cl. Welchii. One aborted incompletely while undergoing treatment with Lugol's iodine for thyrotoxicosis. The uterus was

curetted under nitrous oxide anaesthesia. One week later she underwent operation for sterilisation. She died 40 hours later from auricular fibrillation and hyperpyrexia. The last (aged 37, fifth gravida), admitted with congestive heart failure and anaemia (Hb. 53 per cent) at 20 weeks' pregnancy, was given a successful drug induction when the maximum expected recovery had taken place. Unexpectedly she became maniacal and died from exhaustion.

From the Gynaecological Department 410 patients were discharged. There were 2 deaths. One (aged 66) died from intestinal obstruction some days following radium treatment for confirmed carcinoma corporis uteri. The other (aged 34) died of meningitis (B. proteus) a few days after a Fothergill operation for uterine prolapse. The gynaecological conditions dealt with and the operations performed are enumerated.

Brief reports are given of the work of the pathological and X-ray departments, the sterility clinic, the mobile blood transfusion unit, and the Almoner's department.

Anthony W. Purdie

REPORTS OF SOCIETIES

ROYAL SOCIETY OF MEDICINE

(Section of Obstetrics and Gynaecology)

Meeting held on Friday, February 21st, 1947.

THE evening was devoted to short communications and descriptions of cases by the registrars of hospitals in London and the Home Counties. Dr. Elliot Philipp, Middlesex Hospital, described the treatment of tuberculous salpingitis with special reference to X-ray therapy. Thirteen cases in a series had been treated with X-rays, 12 of them had had laparotomy performed, and 5 had developed a tuberculous sinus following the operation. Within 6 months of the start of X-ray treatment all the sinuses had healed. Treatment involved the giving of very small doses—a total of about 600 r in a course of 12 to 18 treatments, spread over 6 to 9 weeks. From all these cases the only conclusion that could be drawn was that there was as yet no fixed rule for the treatment of tuberculosis in the pelvic organs. Emphasis was put on the importance of rest, good food, heliotherapy, and possible radical surgery.

Dr. Ian Donald, St. Thomas's, described an investigation he had made into the incidence of difficulties in the third stage of labour following the use of Pethidine. His investigations were stimulated by what he termed "a bad run" of manual removal of the placenta. Although only a relatively small number of cases were available, he was able to come to the conclusion that the danger of postpartum haemorrhage could not be ascribed to the use of this substance in the earlier stages of labour.

Mr. Ian Fraser and Dr. Karnicki described cases of full-time ectopic pregnancy. That described by the latter was most remarkable in that a living baby, who survived, was delivered at operation. Dr. Lois Hurter described a case of dysgerminoma of the ovary in a girl of 15. Dr. D. R. Kilgour described a case of carcinoma in the body of the uterus. Dr. R. W. Danziger showed an enormous fibrolipoma, which had grown rapidly from the vulva in a young woman.

Mr. M. Hemans drew attention to the incidence of endometriosis of the cervix. Dr. M. Donald gave the Section a description of a remarkable case of rupture of the uterus. In this patient the uterus ruptured with the final contraction that gave birth to the child, which fact led to considerable difficulty in the making of a diagnosis.

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts of articles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstracters in foreign languages and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of thirty shillings per thousand words.

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ANATOMY

216. **The Pelvic Survey.**
By H. THOMS. *Yale J. Biol. Med.*, **19**, 171–179, Dec., 1946. 10 figs., 8. refs.

217. **Morphology and Histology of the Corpus Luteum.** (Morphologie et histologie des corps progestifs et gestatifs (corps jaunes) de l'ovaire féminin. Modes de degénérescence et reliquats.)
By G. DUBREUIL and M. RIVIÈRE. *Gynécologie*, **43**, 97–127, July–Aug., 1946. 11 figs., 4 refs.

218. **Morphology and Histology of the Corpus Luteum. Processes of Degeneration and Remains.** (Morphologie et histologie des corps progestatifs et gestatifs (corps jaunes) de l'ovaire féminin. Modes de dégénérescence et reliquats.)
By G. DUBREUIL and M. RIVIÈRE. *Gynécologie*, **43**, 129–179, Sept.–Oct., 1946. 12 figs., 125 refs.

PHYSIOLOGY

219. **Histophysiology of the Endometrium; Spiral Arterioles and their Function.** (Contribution à l'histophysiologie de l'endomètre. Les artérioles spiralées. Leur fonction. (Première note).)
By P. ISIDOR. *Gynécologie*, **43**, 193–199, Nov.–Dec., 1946. 10 refs.

PREGNANCY

220. **Uterine Size and Position of the Fundus Uterus during the First Months of Pregnancy.** (Uterusgrösse und Stand des Fundus in den ersten Schwangerschaftsmonaten.)
By F. v. MIKULICZ-RADECKI. *Med. Klinik.*, **41**, 446–448, Oct., 1946. 1 fig.

221. **Does the Ovary Present Cyclic Variations During Pregnancy?** (L'ovaire présente-t-il des variations cycliques pendant la gestation?)
By E. BUJARD. *Rev. méd. Suisse rom.*, **66**, 763–769, Nov. 25, 1946. 16 refs.

222. **Chronaximetric Estimation of Hormones in Gynaecology and Obstetrics.** (Courte note sur l'utilisation en gynécologie et en obstétrique de capachronaximètre: dosage chronaximétrique des hormones.)
By J. COURTOIS. *Gynécologie*, **43**, 211–212, Nov.–Dec., 1946. 2 refs.

223. **Pregnandiol Determinations Made During Last Days of Gestation.** [In English.]
By T. DAHLE. *Acta obstet. gynec. Scand.*, **26**, 627–632, 1946. 4 figs., 4 refs.

Pregnandiol determinations in the urine of 4 pregnant women have been carried out during the last days before delivery. Any noticeable reduction in the pregnandiol secretion has not been proved.—[Author's summary.]

224. **The Effect of Thiouracil Hypothyroidism on Reproduction in the Rat.**
By G. E. S. JONES, E. DELFS, and E. C. FOOTE. *Endocrinology*, **38**, 337–344, June 1946. 2 figs., 2 refs.

Fourteen male and 15 female adult rats had their drinking water replaced by 0.1 per cent thiouracil solution: the average daily intake of the drug was 24 mg. in the males and 20 mg. in the females. Treatment was continued for from 49 to 340 days, and thyroid hyperplasia was produced in all cases. The increase in thyroid weight was greater in the males; the highest weight was 170 mg., against 42 mg. in the females.

Six male rats successfully sired litters after 49 days' treatment, but of 16 attempted matings after 166 to 259 days treatment only 8 were successful. The failures could, however, be attributed to illness, or were in rats which mated successfully in later attempts. There appeared to be some prolongation of the gestation period, which averaged 31 days, excluding two of 57 and 94 days. [No control data of mating or gestation records for the colony are given.]

Nine females treated for 84 days all mated successfully, but 4 resorbed their litters; resorption of litters occurred in all of 18 matings made after 126 to 202 days of treatment.

While the upsets in male fertility are attributed to the general toxic effects of the drug, the resorption of the litters in the females is attributed to the induced hypothyroidism. The mechanism of this effect is discussed, and it is suggested that faulty utilization of oestrogen and/or progesterone in thyroid deficiency leads to a relative deficiency of one or both so that pregnancy cannot be maintained.

Peter C. Williams

225. **Our experience with Falls-Freda and Cohen's Intradermal Reaction for the Diagnosis of Pregnancy.** (Nuestra experiencia con la intrader mo-reaccion calostral de Falls-Freda y Cohen, para el diagnostico del embarazo.)
By D. T. GOROSTIAGA and R. E. LEDE. *Rev. Med. Cien. af.*, **8**, 870–872, Nov. 1946, 5 refs.

226. **Prenatal Examination.** (Examen prénatal.)
By D. MARION. *Union méd. Can.*, **75**, 1372–1379, Nov. 1946. 1 ref.

227. **Prenatal Medical Examination.** (L'examen médical prénatal.)
By E. COUTURE. *Union méd. Can.*, **75**, 1604–1608, Dec. 1946.

228. **The Management of the Toxaemias of pregnancy.**
By J. S. BREWER, G. M. COOPER, E. W. FRANKLIN, J. S. HUNT, T. L. LEE, I. PROCTER, R. A. ROSS, R. A. WHITE, and F. R. LOCK. *North Carolina med J.*, **8**, 31–34, Jan. 1947. 1 fig.

229. **Psychosis in Eclampsia.** (Psicosis eclamptica.)
By F. PEREZ ACOSTA. *Rev. méd.-quirúrg. Orièntе.*, **7**, 147–153. Sept. 1946.

230. **Use of Spasmolytic Drugs in Eclampsia.** (El uso de espasmoliticos en la eclampsia.)
By E. RODERIGUEZ NUNEZ. *Rev. méd. Cubana*, **57**, 626–634, Aug. 1946. 7 refs.

231. **Pathogenesis and Mechanism of so-called Toxic Accidents in Pregnancy.** (Contribution à l'étude de la pathogénie et du méchanisme des accidents dits "toxiques" de la gestation.)
By J. GRASSET. *Rev. franç. Gynéc.*, **41**, 369–393, Dec. 1946.

232. **The Management of Placenta Previa at the Chicago Lying-in Hospital. A Review of 325 Cases during 1931 to 1945.**
By M. E. DAVIS and A. CAMPBELL. *Surg. Gynec. Obstet.*, **83**, 777–788, Dec. 1946.

A careful and detailed summary of a considerable number of cases of placenta praevia treated over a period of years in a large hospital can generally be studied with interest and profit even though, as must usually be the case, no particularly novel or original views as to methods of diagnosis or management are expressed. In this report the management of 325 cases during the years 1931 to 1945 is reviewed. In this series there were only 2 maternal deaths: 1 from haemorrhage shortly after Caesarean section, the other 16 days after operation from sepsis and pulmonary complications—a mortality of 0.6 per cent. The following points are emphasized. There is no treatment of placenta praevia that can be carried out at home; all patients with antepartum haemorrhage after the twenty-eighth week should be admitted to hospital. Vaginal examination should be made only in surroundings where blood transfusions and operative treatment are immediately available. Lower-segment Caesarean section is the best treatment for all cases of central placenta praevia. This operation was done in 121 cases—63 of central and 58 of partial and marginal placenta praevia. The Porro operation was performed for 15 cases. In most cases of incomplete placenta praevia delivery can be completed through the birth passages. Rupture of the membranes is the method of choice, sometimes combined with the use of Willett's forceps (11 cases). Version was performed 15 times, and the bag was inserted 48 times, though the authors now believe that both these methods should be discarded. Tamponade has no place in the treatment. The value of blood and plasma transfusions, supplemented sometimes by intravenous saline, is stressed, as is the importance of having Rh-negative blood or a donor available.

T. C. Clare

233. **A Case of Utero-placental Apoplexy and Placenta Praevia.** (Sobre um caso de apoplexia úteroplacentária e placenta prévia.)
By C. VIEIRA. *Rev. Ginec. Obstet.*, **2**, 188–192. Sept. 1946.

234. **Fifty Cases of Induced Abortion with Reference to the Follow-up of Treated Patients.** (50 Tilfaelde af Abortus provocatus med særligt Hanblik paa Efterundersogelse af de afviste Tilfaelde.)
By G. KRALUND. *Ugeskr. Læg.*, **108**, 1401–1403, Dec. 12, 1946. 1 ref.

235. **Induced Abortion.** (Abortus provocatus.)
By M. A. VAN B. BASTIAANSE. *Tijdschr. soc. Geneesk.*, **25**, 53–61, Feb. 28, 1947.

236. **Embolism after an Attempt at Abortion.** (Apropos d'une embolie après manoeuvre abortive.)
By —. HIRSCH and —. DE TOEUF. *Brux. Méd.*, **27**, 164–168, Jan. 26, 1947. 22 refs.

237. **Hydatidiform Mole versus Chorionepithelioma.** (Môle hydatiforme vs chorioepithéliome.)
By L. GERIN-LAJOIE. *Union méd. Can.*, **75**, 1380–1383, Nov. 1946.

238. **Fibroma and Pregnancy.** (Fibrome et grossesse).
By A. MARMEAUX. *J. Méd. Paris*, **67**, 21, Feb. 1947.

239. **A Case of Chorioepithelioma.** (Corioepithelioma – Caso clínico.)
By L. MAYORGA. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 136–141, Sept. 1946. 3 figs.

240. **A Case of Perforating Chorioepithelioma with Haemoperitoneum.** (Corio-epitélioma perforante. Hemo-peritoneo. Caso clínico.)
By J. ALLAMAND and A. LUCCHINI. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 133–136, Sept. 1946. 5 refs.

241. **Diagnosis and Treatment of Uterine Rupture.** (Diagnóstico y tratamiento de las rupturas uterinas.)
By H. CAICEDO DIAZ. *Med. Cirug.*, **11**, 33–44, Nov. 1946.

242. **Cerebrovascular Complications of Pregnancy.** By W. C. ELLER. *Amer. J. Obstet. Gynec.*, **52**, 488-491, Sept. 1946. 1 fig., 3 refs.

Cerebrovascular complications of pregnancy deserve attention because: (1) gross brain haemorrhage is found in 15 to 20 per cent of necropsies after eclampsia; (2) appreciable brain haemorrhage has a mortality of over 50 per cent and is the second commonest cause of death in eclampsia; (3) areas of softening (encephalomalacia) are relatively frequent, are often unrecognized, and may cause death in the absence of haemorrhage; and (4) patients with sufficient vascular damage to produce fatal haemorrhage or softening should not always be diagnosed as cases of "eclampsia", even in the presence of hypertension, albuminuria, oedema, and convulsions. Three cases are reported.

The first patient, aged 36 years, gravida 9, para 6, had had no antenatal care and was admitted in labour. She had had "fits" with her first pregnancy, but gave no history of hypertension or renal disease; blood-pressure was 195/92, and there was moderate ankle oedema with a trace of albuminuria and a few red-blood cells in the urine. There was uterine inertia. In the next 21 hours she received 2 litres of 5 per cent dextrose in water and sedation with morphine and scopolamine, but the blood-pressure remained elevated, and the temperature rose to 102°F. (38.9°C.); 1 litre of 5 per cent dextrose in water was given by hypodermoclysis. Pulmonary oedema developed, and the patient died in coma 31 hours after admission. Postmortem examination showed generalized slight arteriosclerosis, medial necrosis of the thoracic aorta, perivascular haemorrhage throughout the brain, and an area of 2 cm. in diameter of encephalomalacia in the hypothalmus.

The second patient, a primigravida, had had no antenatal care, and was in labour on admission. She gave no history of hypertensive or renal disease. Blood-pressure was 220/156 and oedema and considerable albuminuria were present. She was delivered spontaneously 4½ hours later of a child weighing 3,041 g. (6 pounds 11 ounces). Blood-pressure fell during labour, but rose 12 hours later, reaching 220/150. Convulsions 19 hours after delivery preceded coma and Cheyne-Stokes respirations with a temperature of 105°F. (40.6°C.). Left hemiplegia and right oculomotor palsy developed. The spinal fluid was under a pressure of 152 mm. of water, contained 188 red blood cells per c.mm. and 224 mg. of protein per 100 ml. The patient died in coma 92 hours after delivery. Postmortem examination revealed a large area of haemorrhage and encephalomalacia in the right mid-brain at the level of the red nucleus just anterior to the cerebral aqueduct and extending to the lower portion of the pons beneath the floor of the fourth ventricle, with very little evidence of chronic arteriolar or renal disease.

The third patient, aged 39 years, para 1, had been treated 2 years previously for a "stroke" and high blood-pressure. It was stated that she complained of pain in the left arm before she fell to the floor. On admission she was comatose; blood-pressure was 246/130; reflexes were equal but hyperactive; the right eye looked down and out. There was no oedema, but there was albuminuria with occasional red blood cells. The spinal fluid was clear under a pressure of 220 mm. of water, with 100 mg. of protein per 100 ml.; later the pressure rose and macroscopic blood appeared. Reflexes gradually disappeared, and hyperpyrexia developed. She died 28 hours after admission. Postmortem examination revealed generalized arteriosclerosis, nephrosclerosis, and cardiac hypertrophy. There was an area 3 cm. in diameter (with surrounding encephalomalacia of indefinite extent) of recent haemorrhage in the mid-brain just above the pons. This patient, in whom the findings and clinical course were similar to those in the other 2 cases, was not pregnant.

Normal blood vessels can withstand a very high pressure over a long period. So with vessel disruption sufficient to produce gross haemorrhage a pre-existing lesion of the vessel wall (such as is seen in essential hypertension, vascular syphilis, or congenital aneurysm) might be expected. But in true pre-eclampsia and eclampsia reversible vasospasm is the only vascular lesion. The third case illustrates the fact that the chronic vascular changes are not peculiar to pregnancy. The second patient showed none of these chronic vascular changes. It is suggested that the temporary vasospasm produces an area of softening distal to the point of spasm. In the area of softening thus produced the vessel itself may undergo softening and subsequent disruption and haemorrhage. At any rate, encephalomalacia itself of sufficient extent or in a suitable place may have a fatal result. The

importance of neurological examination in the toxaemic patient is stressed. This point is not purely academic. Certain intracranial haemorrhages are amenable to possible life-saving surgical treatment. *Anthony W. Purdie*

243. **Pyelourereteritis in Pregnancy.** (Pielourereteritis gravidica.)
By A. J. GUIROY and F. A. URANGA IMAZ. *Prensa med. argent.*, **34**, 97–102, Jan. 10, 1947.

244. **Impregnation, Pregnancy and Diabetes.** (Fecundación, embarazo y diabetes.)
By M. ESPEJO and G. DE AVELLANEDA. *Actualid. méd. Granada*, **22**, 705–708, 1946.

245. **Heart Disease in Pregnancy.**
By B. E. HAMILTON. *J. Missouri med. Ass.*, **44**, 17–21, Jan. 1947.

246. **The Heart and Vitamin B_1 Deficiency in Pregnancy.** (Cuore ed ipovitaminosi B_1 in gravidanza.)
By F. DE MATTEIS and E. ROBECCHI. *Minerva med. Torino*, **1**, 201–204, Feb. 17, 1947. 3 figs.

247. **Coarctation of the Aorta in Pregnancy.** (Isthmusstenose en zwangerschap.)
By G. A. LINDEBOOM. *Ned. Tijdschr. Geneesk.*, **91**, 155–157, Jan. 18, 1947. 4 refs.

248. **Chylothorax: Pregnancy in an Arrested Case.**
By G. EDLUND *Minn. Med.*, **30**, 47–48, Jan. 1947. 5 refs.

249. **The Action of Penicillin on the Guinea-Pig Uterus.** (Action de la pénicilline sur la corne utérine du cobaye.)
By J. PELLERAT and —. MURAT. *Ann. Derm. Syph.*, **6**, 363–364, May–June, 1946. 1 ref.

The possibility of abortion due to the action of penicillin on the pregnant uterus has been suggested, as in pregnant women treated with penicillin for gonorrhoea spasmodic uterine pains have been reported. Penicillin in a dose of 0.5 units per ml. was found to cause contraction of the isolated guinea-pig uterus, whereas this dose has no action on the isolated intestine. The concentration of penicillin which produces uterine contractions *in vitro* corresponds to that obtained in the blood *in vivo* after an intramuscular injection of 20,000 units. *G. M. Findlay*

250. **Origin, Course and Symptomatology of Intraligamentous Pregnancy.** (O postanku, razvitku i simptomatologiji intraligamentoznog graviditeta.)
By F. DRAZANCIC. *Lijecn. Vjesn.*, **68**, 227–232, Dec. 1946. 2 figs., 15 refs.

251. **Vesical and Renal Symptoms in Interrupted Extrauterine Pregnancy.** (Sintomi vescicali e sintomi renali nella gravidanza extrauterina interrotta.)
By B. SORRENTINO. *G. ital. Chir.*, **2**, 539–550, Dec. 1946. 3 figs., 10 refs.

252. **Repeated Ectopic Pregnancy.**
By H. BRYAN and T. J. MONTEMURO. *Canad. med. Ass. J.*, **55**, 601–602, Dec. 1946. 3 refs.

253. **Two Cases of Interstitial Ectopic Pregnancy.** (Sobre dois casos de gravidez ectopica intersticial.)
By H. MACHADO HORTA. *Rev. Ginec. Obstet.*, **40**, 296–301, Nov. 1946. 3 figs.

254. **Vagitus Uterinus. Report of Two Cases.**
By G. A. BOURGEOIS and H. L. KING. *Bull. U.S. Army med. Dept.*, **7**, 147–148, Jan. 1947. 1 fig., 2 refs.

LABOUR

255. **Prognosis in Labour.** (Pronostico del parto.)
By D. J. MILLAN SANTOS. *Toko-ginec. pract.*, **5**, 371–380, Nov. 1946.

256. **Use of Calcium-quinine in Clinical Obstetrics.** (El empleo de la quinina-calcio en la clinica obstetrica.)
By J. BOTELLA LLUSIA, A. PEREIRA MARTINEZ, and J. GARCIA DEL ALAMO. *Medicina, Madrid*, **14**, 361–392, Nov. 1946. 29 figs., 28 refs.

257. **Polycystic Disease of Kidneys Causing Dystocia. Review of the Literature and Report of a Case.**
By J. W. BOURLAND. *Urol. cutan. Rev.*, **50**, 669–670, Nov. 1946. 8 refs.

258. **Foetal Ascites Obstructing Labour.** (Foetaler Ascites als Geburtshindernis.)
By K. MAGYAR. *Gynaecologia*, **122**, 363–370, Dec. 1946. 6 figs.

259. **Sympatheticomimetic Amines in Labour.** (Le amine simpaticomimetiche nel travaglio del parto.)
By G. P. BALASSI. *Ginecologia, Torino*, **12**, 297–306, Oct. 1946. 34 refs.

260. **Results of the Use of Compositrine in Connection with Danger to the Foetus.** (Uitkomsten van het gebruik van compositrine [ermetrine compositum] bezien in verband met gevaren voor het kind.)
By B. S. TEN BERGE and G. LINTHORST. *Ned. Tijdschr. Geneesk.*, **90**, 1723–1731, Nov. 23, 1946. 2 figs., 6 refs.

261. **Management of Breech Delivery.** (Acerca da assistência ao parto de nádegas.)
By M. QUEIROZ DE BARROS. *Rev. Ginec. Obstet.* **2**, 143–153, Sept. 1946. 2 figs., 52 refs.

262. **Bracht's Method in Breech Presentation.** (La maniobra de Bracht en el parto podálico. [Nota previa sobre una experiencia personal de 26 casos].)
By N. O. DI FONZO. *Rev. méd.-quirúrg. Pat. fem.*, **25**, 392–399, Sept. 1946. 4 figs., 9 refs.

263. **Prognosis and Management of Labour in Breech Presentation in Cases of Pelvic Contraction.**

(Prognosi e terapia del parto in presentazione podalica nei bacini limite.)

By P. L. BIANCHI. *Ginecologia, Torino*, **12**, 307–322, Oct., 1946. 20 refs.

264. **Transverse Presentation.**

By J. T. COLE and F. DELANY. *Surg. Gynec. Obstet.*, **83**, 473–479, Oct., 1946. 18 refs.

The authors report 78 cases of persistent transverse presentation occurring in 45,000 deliveries at the Women's Clinic of the New York Hospital between 1932 and 1946. Their purpose is to present a recent series of cases and to evaluate the influence of advances in surgery, chemotherapy, and blood transfusion in the choice of treatment. Their series differs from others in that in as many as 46 per cent of cases delivery was by Caesarean section, with no maternal or foetal deaths. The paper opens with a short review of well-known papers on treatment from the mid-eighteenth century down to recent years. Then comes a brief account of the probable aetiological factors in the authors' series. One maternal death (1.3 per cent) and 18 foetal deaths (23 per cent) occurred in the whole series. Investigation revealed that 7 foetal deaths occurred before the onset of labour, 8 were associated with labour and delivery, and 3 were neonatal deaths. In the 58 cases in which the foetal heart was audible on admission and the foetus weighed 2.5 kg. or more only 5 foetal deaths occurred (8.6 per cent). The one maternal death (associated with placenta praevia and ruptured lower segment) is recorded in detail. Treatment is discussed at some length. The high mortality figures (both maternal and foetal) that accompany delivery from below, and the complications that arise from unwise internal version and breech extraction, are emphasized. The intelligent evaluation of the individual case must, naturally, always be made; but, in the authors' view, the more frequent use of Caesarean section is indicated by the low mortality figures.

[The authors present their evidence well and argue their case clearly. The fact is inescapable that modern technical advances have greatly increased the safety of Caesarean section and have justifiably widened its indications.]

Eardley Holland

265. **Uterine Inversion.** (Inversão uterina tocogenética.)

By F. COTTA PACHECO. *Rev. Ginec. Obstet.*, **2**, 164–186, Sept. 1946. 5 figs., 24 refs.

266. **Post-partum Intra-abdominal Separation of Uterus.**

By J. J. S. WASSENAAR. *Brit. med. J.*, **1**, 452, Apr. 5, 1947. 1 fig.

ANAESTHETICS, ANALGESICS

267. **Anaesthesia and Analgesia in Childbirth.**

By C. R. S. COLLINS. *J. nat. med. Ass.*, **39**, 26–31, Jan. 1947. 15 refs.

268. **Local Infiltration Anaesthesia in Obstetrics and Gynaecology.** [In English.]

By J. P. GREENHILL. *Gynaecologia*, **122**, 309–326, Dec. 1946. 5 refs.

269. **Continuous Spinal Anaesthesia in Obstetrics.**

By R. E. GILLETT. *Northw. Med.*, **45**, 743–747, Oct. 1946. 24 refs.

The author's technique of continuous spinal analgesia in labour is described. The third or fourth lumbar interspace is selected for lumbar puncture. After preliminary puncture of the skin with a Sise introducer a malleable spinal needle is introduced; it is then fixed to the skin with strips of adhesive tape and allowed to remain *in situ*. Gauze soaked in antiseptic solution is wrapped around the shaft of the needle and the latter is connected by rubber tubing with a stopcock and syringe containing the anaesthetic agent. A special mattress provided with a cut-out space which accommodates the needle and tubing and allows the patient to lie on her back is essential. Anaesthesia is usually started as soon as uterine contractions are well established and pain is sufficient to justify its use. Pethidine intramuscularly or a barbiturate by mouth reduces apprehension, and 50 mg. of ephedrine by intramuscular injection is given prior to lumbar puncture.

"Pontocaine" (amethocaine hydrochloride) was used in 450 cases and "metycaine" in 50, and both were mixed with 10 per cent dextrose solution to produce a hyperbaric solution. The concentration of drug in each millilitre of this mixture was either 2 mg. of pontocaine or 15 mg. of metycaine. The volume of each injection was usually 2 ml., but in some instances this amount was increased to 3 ml. or reduced to 1 ml. All injections were made slowly and without barbotage and the height of anaesthesia was controlled by varying the position of the patient. The length of anaesthesia was readily prolonged by repeating the injection as required. Pulse-rate and blood-pressure were taken

at 5-minute intervals for the first half-hour following injection. The urinary bladder was observed, and catheterized immediately if it showed signs of distension. The spinal needle was removed before the patient was placed in her final position for delivery. A small injection gave adequate anaesthesia for delivery. Caesarean section could be performed under the same analgesic. Contraindications were: (1) Low blood-pressure; systolic 90 mm. and diastolic 50 mm. were considered the lowest limits. (2) Marked anaemia or actual or potential haemorrhage. Disease of the nervous system, infection at the site of contemplated puncture, emotional instability, or fear of spinal analgesia must also be considered.

Satisfactory analgesia was obtained in 95 per cent of cases. Only 1 case in 5 was delivered without some form of operative intervention. Episiotomy was performed in over two-thirds of the cases. No deaths were attributable to the analgesic. In only 36 per cent of cases was the drop in blood-pressure insignificant. Treatment was by injection of 4 minims (0.25 ml.) of 1:1,000 adrenaline solution in one case where the blood-pressure fell to zero. In the less severe cases of hypotension repeated intravenous ephedrine was found effective; the quantity and frequency of injections are not stated. The average duration of analgesia was 3½ hours for multiparae and 5 hours for primiparae; the longest was 24 hours.

John Challis

270. **Caudal Analgesia for Obstetrics in Private Hospital.**

By J. D. KINDSCHI. *Northw. Med.*, **45**, 747–750, Oct. 1946. 3 refs.

Initial trials with caudal analgesia were unsatisfactory owing to faulty technique of needle insertion. Unilateral anaesthesia, drop in blood-pressure, and other discouraging results were obtained, and out of 15 cases only 3 were successful. In a series of 275 cases there were 5 with marked reactions. These were of two types: (1) In 1 case circulatory collapse was corrected by oxygen inhalations and ephedrine administration. (2) In 4 cases the level of anaesthesia was pushed too high; this complication was treated by ephedrine and pituitrin. "Metycaine" 1.5 per cent in Ringer's solution was used in all cases, the largest dose being 75 ml. and the smallest 38 ml., with an average of 65 ml. for multiparae and 95 ml. for primiparae. A 19-gauge malleable needle was used and discarded after 10 cases.

In a further series of 1,003 cases there was only 2.5 per cent of failures. Labour was induced in the great majority of cases, and in well over a half low forceps extractions were performed. Complications included a drop in blood-pressure of at least 40 mm. in 10 cases, foetal death in 1 case, maternal death in 1 case, and entry of the dural sac in 2 cases. In the event of puncture of the dural sac caudal analgesia was immediately discontinued. The maternal death was not attributable to the caudal block; the foetal death occurred in a case where the anaesthesia rose to the level of the third dorsal segment with concomitant circulatory depression and anoxia of both mother and foetus.

It is recommended that oxygen, plasma, ephedrine or "methedrine", intravenous barbiturate, "coramine" or caffeine, and sterile spinal needles should always be immediately available. "Multiparas are injected when 3 to 4 cc. [*sic*] dilated and primiparas at 4 to 5 cc. . . . in the prone or modified knee-chest position with a pillow at the pelvis." A barbiturate may be administered first. As after 6 to 8 hours the anaesthesia diminishes and slight toxic effects are evident, it is not advisable to start anaesthesia too soon. Five to 10 minutes after giving the test dose of 8 ml. of the solution an additional 20 to 40 ml. is added and the patient is turned on her side. This will bring the level of anaesthesia to the eleventh or twelfth dorsal segment. If the level extends higher on the dependent side after a period of 10 to 15 minutes she is turned over and the procedure is continued with additional 15 to 20 ml. doses at intervals of 30 to 45 minutes as indicated by the level of anaesthesia determined by pin-prick on the abdominal wall or by return of pain. When the patient is ready for delivery the final injection is made to assure an upper level of anaesthesia at or above the umbilicus and the needle is withdrawn. Sulphathiazole ointment and a dressing are applied. In multiparae the perineum and vulva must be watched to anticipate precipitate delivery. The second stage of labour is usually terminated by forceps and episiotomy. Infection at the site of injection did not occur in any of the cases reported. Postpartum care is simplified, and patients are discharged on the eighth day.

John Challis

271. **The Management of Complications Arising from the Use of Caudal Anesthesia in Obstetrics.**
By P. E. HENDRICKS. *J. Bowman Gray Sch. Med.*, **4**, 175–183, Nov. 1946. 44 refs.

272. **The Aspiration of Stomach Contents into the Lungs during Obstetric Anaesthesia.**
By C. L. MENDELSON. *Amer. J. Obstet. Gynec.*, **52**, 191–205, Aug. 1946. 20 figs., 3 refs.

The incidence of aspiration of stomach contents into the lungs was 0.15 per cent in 44,016 cases of anaesthesia for obstetrics. The anaesthetic was a mixture of gas, oxygen, and ether in all instances. The aspirated material was liquid in 40 cases and solid in 5; of the latter, 3 patients (2 of whom died) had complete respiratory obstruction, while the remaining 2 had incomplete obstruction with massive atelectasis; both recovered on coughing up the obstructing material. Cyanosis, tachycardia, and dyspnoea were present, with signs of massive collapse, mediastinal shift, and consolidation. The 40 cases of aspiration of liquid material had cyanosis, tachycardia, and dyspnoea, but there was no massive atelectasis or mediastinal shift. On ausculation, wheezes, rales, and rhonchi, were heard. A pulse-rate of 160 and a respiration-rate of 40 were common. X-rays showed irregular soft mottled densities in the involved areas, but no mediastinal shift. The patients were critically ill during the acute period, but the condition became gradually stabilized within 24 to 48 hours. Films showed complete recovery in 7 to 10 days. Right lungs were more commonly involved, but massive aspiration involved both lungs. Many cases occurred before the introduction of sulphonamides and penicillin. Experimental work on rabbits bore out the results found in clinical cases. Infection is relatively infrequent, but when it does occur it is a serious complication. During labour the stomach empties very slowly, and food taken 24 to 48 hours before may be vomited. Points in prophylaxis and treatment are: (*a*) withholding oral feeding during labour; (*b*) use of local analgesia where possible; (*c*) alkalinization of and emptying of stomach contents prior to general anaesthesia; (*d*) provision of skilled anaesthetists and of adequate equipment for postural and bronchial drainage; (*e*) prompt recognition and treatment of the condition. *John Challis*

See also No. 305.

PUERPERIUM

273. **A Case of Hypophyseal Atrophy in the Puerperium.** (Un caso di insufficienza ipofisaria post-partum.)
By L. VIALE. *Arch. "E. Maragliano," Pat. Clin.*, **1**, 368–376, Nov.–Dec. 1946. 30 refs.

274. **Postnatal care of the Venous System.** (Algunos aspectos sobre la revision y cuidados del sistema venoso en el postparto.)
By L. ABAD COLOMER. *Toko-ginec. Pract.*, **5**, 381–391, Nov. 1946.

275. **Vaginal Malformations and the Puerperium.** (Malformaciones vaginales y estado puerperal.)
By R. GARCIA PASTOR. *Toko-ginec. Pract.*, **5**, 357–370, Nov. 1946. 5 figs., 10 refs.

276. **Behaviour of Urinary Elimination of Trimethylamine in the Puerperal State.** (Comportamento dell' eliminazione urinaria di trimetilamina nello stato puerperale.)
By G. COLUCCI. *Ginecologia, Torino*, **12**, 323–330, Oct. 1946. 2 figs., 15 refs.

THE INFANT

277. **Statistics of Births and Premature Births in the Foreign Paediatric Literature (1940-1945).** (Nouveaunés et prématurés dans la littérature pédiatrique étrangère [1940-1945].)
By — SCHACHTER. *J. méd., Paris*, 169–172, Nov. 1946. 4 refs.

278. **Hydrocephalus in a Maternity Home.** (La hidrocefalia en el Instituto de Maternidad.)
By F. URANGA IMAZ, R. DUBROVSKY, and P. ALBANESE. *Prensa méd. argent*, **33**, 2038–2041, Oct. 4, 1946. 7 refs.

279. **Anoxia Neonatorum.**
By C. L. SULLIVAN. *New. Engl. J. Med.*, **235**, 894–896, Dec. 19, 1946. 4 refs.

280. **Shortness of the Neck in the Newborn (Cases of Klippel-Feil Syndrome).** (I neonati senza collo. Contributo casistico sul morbo di Klippel-Feil.)
By G. VECCHIETTI. *Clin. Ostet. Ginec.*, **48**, 235–245, Nov.–Dec. 1946. 6 figs., 45 refs.

281. **Notes on an Outbreak of Pemphigus Neonatorum in a Private Nursing Home.**
By G. C. WILLIAMS, C. SIMS-ROBERTS, and G. T. COOK. *Mon. Bull. Min. Health*, **6**, 13–20, Jan. 1947. 10 refs.

A nursing home, well situated, with 20 beds all in large, well-ventilated, single rooms, but with only one labour ward, one sterilizing room, a small nursery, no milk kitchen, and no separation unit,

was the scene of the outbreak of pemphigus neonatorum. The bookings were limited and the average stay in the home was 14 days. The staff was adequate.

In the discussion the authors refer to a number of points of interest revealed by the investigation. Each patient had her own private practitioner in attendance and " the list of doctors was a formidable one." There was no scheme whereby the staff could be made aware of any abnormal circumstances in connexion with the different cases in the home, and each practitioner had his or her own ideas about the management of cases. General conditions in the home were excellent. Sufficient evidence was found to account for spread; for example, there was no dry-sterilization of masks and there were no facilities for drying napkins or for " dry-sweeping " the floors. Although the lesions were mild the results of swabbing showed a wide distribution of *Staphylococcus aureus* in the community. Bacteriophage typing was of great value in detecting the " epidemic strain ".

R. H. Parry

282. **Haemolytic Jaundice.** (Ictericia hemolitica.)
By O. L. MARRUGAT and R. A. LAGRANDA. *Rev. med.-quirúrg. Pat. fem.*, **25**, 400–410, Sept. 1946.

283. **The Feeding of Infants, with special reference to Premature Babies.** (Beitrag zur Neugeborenen-Ernährung unter spezieller Berücksichtigung der Frühgeburten.)
By V. MORF. *Ann. Pædiat., Basel*, **168**, 40–56, Jan. 1947. 3 figs., 10 refs.

284. **The stillbirth-rate in England and Wales in Relation to Social Influences.**
By I. SUTHERLAND. *Lancet*, **2**, 953–956, Dec. 28, 1946. 7 refs.

Between 1929 and 1940 the stillbirth-rate for England and Wales decreased only 5 per cent and deaths per 1,000 live births at ages under 4 weeks decreased 10 per cent, while the death-rate at ages 9 to 12 months decreased 48 per cent. The author makes a regional comparison for 1929–40; the London boroughs had the lowest and Wales (all types of area) the highest rates. Only in Scotland is a statement of the supposed cause of stillbirth required on the certificate. The return for 1943 assigned 33 per cent to difficulties in labour and accidental haemorrhage and 19 per cent to " ill-defined and unknown causes." The stillbirth-rate for a constant age is highest in nulliparae but begins to rise again after the first birth; there is a steady increase with age for all degrees of parity. As, however, there has been a considerable decrease in the stillbirth rate, especially since the war—in Wales the rate fell by 34 per cent and in England by 27 per cent between 1938 and 1944—factors of social-economic order must also be involved. During the war the environment of pregnant women deteriorated in many respects but the stillbirth-rate fell.

Two social-economic factors, however, improved —nutrition and antenatal care. A test of this explanation is to see how well the stillbirth-rate can be expressed in terms of other social-economic indices by means of a regression equation. The author used five, the crude birth-rate, the proportion of occupied males over 14 in social classes iv and v, mortality-rate of 3 to 12 months, number of persons per room in private families, and the percentage of occupied males out of work. The data related to the pre-war period. The result was, in the more favourable case (the county boroughs of England and Wales), to improve the accuracy of the estimate by about 30 per cent. [If all we know is the mean stillbirth-rate for a set of county boroughs, the best estimate we can give for each is the mean of all; but if we know the values of the five indices for each borough we should substitute a different estimate in each instance, unless, of course, the values of the indices were the same; the result would be that the square root of the average of squared deviations of predicted from observed in the second case would be about 30 per cent smaller than in the first. In other words, the indices chosen did not cover more than a moderate proportion of the factors on the stillbirth-rate].

Major Greenwood

285. **A Rare Cause of Foetal Death.**
By P. P. KIRWAN. *Brit. med. J.*, **1**, 297, Mar. 8, 1947.
Rh factor, erythroblastosis foetalis.

286. **Permeability of the Human Placenta to Iso-antibodies.**
By A. S. WIENER. *J. Lab. clin. Med.*, **31**, 1020–1024, Sept. 1946. 15 refs.

Rh-negative individuals sensitized to the Rh factor may produce either or both of two sorts of antibodies—Rh agglutinins and Rh-blocking antibodies. The presence of Rh agglutinins can be demonstrated by direct testing in saline media, while the presence of Rh-blocking antibodies can

be demonstrated either by the so-called blocking test performed in a saline medium—that is, the demonstration that Rh-positive cells exposed to the blocking antibody became inagglutinable by agglutinating antibody—or directly by excluding crystalloids and performing the test in a protein solution. It is postulated that protein media contain a third component—"conglutinin," probably a colloidal aggregate of plasma protein. If this hypothesis is correct, Rh glutinins (blocking antibodies) must be smaller molecules than Rh agglutinins, and might then prove to pass through the placenta more readily than agglutinins.

In order to test the validity of the hypothesis the author decided to see whether the same considerations applied to immune anti-A and anti-B antibodies. Two special cases of iso-immunization to the Rh agglutinogen were investigated; both were mild cases of erythroblastosis foetalis in which there was no incompatibility between mother and foetus with regard to the Rh factor but in which the damage to the foetal erythrocytes (group A) appeared to be due to the formation by the mother (group O) of immune anti-A antibodies. Sera of mother and infant were examined and comparative titrations of anti-A and anti-B antibodies carried out in saline and serum. These showed that, whereas the anti-B titres in saline were higher in the mother's serum (8 and 64 times respectively), when titrated in serum, the anti-B reactions were equally strong in the infant's serum. This seems to show that the mothers have two kinds of antibody in their sera, and that the kind which reacts only in protein media passes through the placenta more readily. The anti-A titres in the mother's sera were equally great when tested in saline and in serum; no anti-A antibodies could be detected in the infants' sera by either technique. It is suggested that the anti-A "glutinins" in the mothers' sera constantly passed through the placenta during pregnancy in these 2 cases, and were absorbed by group substances in the group A foetus's body, thus gradually depleting the mother's body of anti-A antibodies.

P. L. Mollison

287. **Recent Developments in the Knowledge of the Rh-Hr Blood Types; Tests of Rh Sensitization.**
By A. S. WIENER. *Amer. J. clin. Path.*, **16**, 477–497, Aug. 1946. 2 figs., 73 refs.

This is a review of the author's work on the "theory, heredity, and anthropologic applications of the Rh-Hr blood types, and also of the newer tests for Rh sensitization". He summarizes his hypothesis that the congenital erythroblastoses comprise 3 "distinct, though related, clinical diseases": (1) icterus gravis neonatorum, due to maternal anti-Rh agglutinins "milked" into the infant's circulation during labour; (2) congenital haemolytic disease due to "univalent Rh antibodies (Rh blockers or glutinins)" transmitted to the foetus during pregnancy; (3) icterus praecox, due to maternal alpha or beta antibodies acting on incompatible foetal red cells.

[This paper should be consulted by those interested in Rh; that it is itself an abstract of a prodigious amount of work is indicated by reference to 47 papers written by the author and his collaborators, mostly between 1943 and 1946. The author's views on aetiology of the different forms of erythroblastosis have met with some criticism. In dealing with the "newer tests for Rh sensitization" no mention is made of the two most important recent contributions to this aspect of Rh work—Diamond's albumin test (1945) and Coombs' rabbit anti-globin test (1945).]

R. R. Race

288. **The Rh Factor as Applied to the Operation of Blood Banks.**
By L. J. UNGER, M. WEINBERG, and M. LEFKON. *Amer. J. clin. Path.*, **16**, 498–505, Aug. 1946. 1 fig., 6 refs.

The problem of choosing donors and recipients for Rh grouping is discussed, and it is concluded that the simplest and safest procedure is to group them all. During 1945, 22,631 donors to the blood bank of the New York Post-Graduate Medical School and Hospital were Rh-grouped. Of these "14.7 per cent were Rh-negative, 1 per cent type Rh′, 0.6 per cent type Rh″, and 0.004 per cent type Rh′Rh‴". Anti-Rh_0 serum was used [anti-D of English workers]. Blood negative with this serum was subsequently tested with anti-Rh′ [anti-C] and anti-Rh″ [anti-E] sera. The rapid slide test of Diamond and Abelson (*J. Lab. clin. Med.*, 1945, **30**, 204), using oxalated whole blood and "blocking" anti-Rh_0 serum, was found to be completely satisfactory. Figures given for the results of comparative tube tests support this claim.

[The authors state that 1 in 25 Rh-negative

persons transfused with Rh-positive blood becomes sensitized. Now that more sensitive tests for immunization are available it is thought that the proportion is much higher.] *R. R. Race*

289. **The Rhesus Factor in Indians.**
By G. W. G. Bird. *Antiseptic*, **43**, 645–646, Oct. 1946. 2 refs.

The blood of 390 Indian soldiers, " of all religions and castes, and belonging to all parts of India ", was tested with human anti-D (anti-Rh_0, 85 per cent) serum; 386 subjects, or 98.9 per cent, were Rh positive. The proportion of Rh-negatives was lower than that found by other investigators who had used animal anti-Rh serum. [The results using serum of human origin should be the more reliable.]

The tests were performed in tubes, and the presence of agglutination was determined by naked-eye examination of the cell deposit. [A microscopical examination of the cell deposit, pipetted on to a slide, is more trustworthy.] " The serum was that known as anti-Rh (synonyms: anti-Rh 85 per cent, anti Rh_0, anti-D, etc.), i.e., it was identical with the serum which Landsteiner and Wiener first discovered in 1940 by injecting the red-blood corpuscles of Rhesus monkeys into rabbits or guinea-pigs."

[This is an error widely held. The human antiserum now called anti-Rh_0 or anti-D was discovered by Levine and Stetson in 1939 (*J. Amer. med. Ass.*, 1939, **113**, 126), but was, perhaps unfortunately, given no name by the discoverers. When the rabbit anti-rhesus-monkey antibody, discovered by Landsteiner and Wiener in 1940, was found to give, up to a point, the same reactions as the human serum, the antibody in the latter became known as anti-Rh.] *R. R. Race*

290. **Some Observations Upon the Rh Factor in Pregnancy.**
By C. H. Ingram. *Amer. J. Obstet. Gynec.*, **52**, 440–445, Sept. 1946. 12 refs.

In the obstetric service of the Western Pennsylvania Hospital during the first 15 months after routine Rh determinations and kindred studies were started, 6 cases of erythroblastosis foetalis were encountered in 1,682 deliveries—1 case per 280 deliveries. They resulted from delivery of 75 Rh-negative women (incidence of 1 in 12.5 Rh-negative women). Of 1,129 Rh determinations 10.36 per cent proved Rh-negative. Landsteiner and Wiener gave the incidence as 15 per cent among white subjects. More important probably than the inclusion in this series of a few negroes is the fact that the original work classes Rh' and Rh" as negatives while now they are classed among Rh-positive groups.

The series is small, but certain facts have been observed and impressions have been formed. These are listed in the hope that, with the experience of others, they may be helpful in the future management of Rh-negative mothers and their babies. (1) An Rh determination should be carried out on all pregnant women. In this series 4 babies have been salvaged who otherwise would have been lost. (2) A careful history of previous transfusions, as well as of pregnancies, should be taken in all Rh-negative pregnant women. If possible the donor's blood should be tested for the Rh factor before delivery. Only Rh-negative blood should be given to any Rh-negative woman who has not reached the end of her reproductive life. (3) All Rh-negative multigravidae and those who have been transfused either with Rh-positive or unknown blood should be tested for agglutinins and blocking antibodies at least once during the last 3 months of pregnancy. (4) In cases with either marked agglutination or blocking reaction preparations should be made for a full study of the infant's blood in the delivery room. If the red-cell count is 2,500,000 or less Rh-negative blood should be given by the umbilical vein before the cord is tied. (5) Whenever transfusion is indicated for the baby Rh-negative blood should be used. The author has contemplated using a suspension of washed maternal cells, but has never been forced to do so. (6) Once the cord is tied the method of administration found most useful is by a 22-gauge cannula into a surface vein, pressure being supplied by a syringe. In one case where cannula and vein had become obstructed and the baby was exhausted from transfusion efforts 75 ml. of blood was given intraperitoneally. The final result was satisfactory, though the baby displayed mild shock shortly afterwards. The author hesitated to use this routine again because of the shock. (7) Infants with erythroblastosis should not feed at the breast as breast milk contains anti-Rh agglu-

tinins. (8) Prognosis in affected babies must remain guarded in view of neurological residua such as spasticity and mental retardation attributed to kernicterus and reported by, among others, Leonard and Docter. The author's patients until the present have continued to be satisfactory. (9) The outlook for future babies appears to depend on 2 factors: first, another baby may be Rh-negative with no sign of trouble; secondly, even if it is Rh-positive it may survive with treatment. This latter outcome is more likely if pregnancy is postponed at least until the maternal blood is free from agglutinins and blocking antibodies. (10) The margin of safety is slender with full-term babies. Induction of premature labour means the added risks of prematurity. For this reason it is opposed.

[While agreeing that the intraperitoneal route is not ideal, the abstracter has also given blood on one occasion to an infant with erythroblastosis when accidents had befallen each accessible vein. The result here, too, was eminently satisfactory: cf. (*a*) Siperstein and Sansby (*Amer. J. Dis. Child.*, 1923, **25**, 107), and (*b*) Hahn *et al.*, (*J. Exp. Med.*, 1944, **80**, 77).] *Anthony W. Purdie*

291. **The Rh Types in Canadians of Japanese Race.** By B. CHOWN, Y. OKAMURA, and R. F. PETERSON. *Canad. J. Res.*, **24**, Sect. E, 135–143, Oct. 1946. 30 refs.

The authors collected samples of blood from 606 Japanese persons living in Canada. The samples were tested with the Rh sera anti-D, anti-C, anti-E, and anti-c. This was the first time that Japanese bloods had been so fully examined. As many of the 606 bloods were from related persons, the calculations of the gene frequencies were based on 217 samples, picked out of the larger number, believed to be from unrelated people. The following table gives the number and frequency of Rh phenotypes based on reactions with 4 antisera:

Reaction with antisera					Entire sample		Sample of unrelated individuals	
D	C	E	*c*	Phenotype	Number	Frequency	Number	Frequency
+	+	+	+	R_1R_2	252	0.4158	95	0.4378
+	+	–	–	R_1	205	0.3383	73	0.3364
+	–	+	+	R_2	78	0.1287	27	0.1244
+	+	–	+	R_1r	62	0.1023	20	0.0922
–	–	+	+	R''	6	0.0099	1	0.0046
+	+	+	–	R_z	2	0.0033	1	0.0046
–	–	–	+	*r*	1	0.0017	—	—
					606		217	

The authors' figures for the gene or chromosome frequencies were: R_1 (CDe), 58 per cent; r (cde), 7.95 per cent; R" (cdE), 2.89 per cent; R_z (CDE), 0.40 per cent; and R_2 (cDE), 30.76 per cent. It was thought that the frequencies of R_0 (cDe), R' (Cde), and R_y (CdE) were either zero or very small indeed. Comparing the observed frequency of bloods in the R_1R_2 and R_2r groups with the expected frequency, calculated from the above gene frequencies, an excess of R_1R_2 and a shortage of R_2r was disclosed. The authors consider that if their anti-C serum contained a small amount of anti-D as well, then homozygous R_2R_2 (cDE/cDE) blood may have been scored as R_1R_2.

R. R. Race

292. **Inheritance of the Allelomorphs of the Rh Gene in Canadians of Japanese Race: A Study of 65 Families.** By B. CHOWN, Y. OKAMURA, and R. F. PETERSON. *Canad. J. Res.*, **24**, Sect. E., 144–147, Oct. 1946. 9 refs.

The results of the Rh grouping of 64 Japanese families (plus one from which the father is missing) and 176 of their children are classified according to the type of mating and the group of the offspring. The details of individual families are not given. The bloods were all tested with anti-C, anti-D, anti-E, and anti-c. This was the first time in which families other than European had been tested with these 4 anti-Rh sera. The authors conclude: "The data obtained were in agreement with R. A. Fisher's hypothesis of the allelic Rh genes. No exceptions to expected results were obtained." The sera used in the investigations were provided by Dr. Diamond and by Dr. Vogel.

[In this and the preceding paper the presentation is admirable. The authors have succeeded in making it clear when they are speaking of phenotypes and when of genotypes. They have also made clear which genotypes they expect the phenotypes in their population to include. The notation employed is the CDE of Fisher, together with the shorthand names in use in England; for example, R_1 for CDe, R_2 for cDE, r for cde.]

R. R. Race

293. **The Use of Heparin when Performing Exchange Blood Transformations in Newborn Infants.** By A. S. WIENER and I. B. WEXLER. *J. Lab. clin. Med.*, **31**, 1016–1019, Sept. 1946. 1 fig., 10 refs.

The authors believe that the syndrome of icterus gravis neonatorum is initiated by intravascular agglutination, and that therefore the removal of Rh-positive cells and their replacement by Rh-negative cells may be expected if carried out early enough to prevent the development of the syndrome or, if given later, to arrest its development. Mathematical considerations show that if blood is injected and withdrawn at the same rate and in the same quantities the following degrees of replacement will be effected. If an amount equal to the infant's blood volume is injected there will be 63 per cent of donor's blood in its circulation at the end. If an amount equal to twice the infant's blood volume is injected the proportion of donor blood will rise to 86 per cent. The amount must be increased to 3 times the infant's blood volume to obtain a 95 per cent replacement. Since the infant at birth has a blood volume of approximately 250 ml., little will be gained by a transfusion of more than 500 ml. The following technique is recommended:

The internal saphenous vein is exposed at the ankle and a blunt 20-gauge cannula is tied into place with catgut; 0.5 ml. of heparin (500 units) is injected through the needle, and blood is then allowed to run in. An incision is made at the wrist and a short-bevel 20-gauge needle is inserted into the radial artery. This needle is not inserted until the infant has already received the first 50 ml. of the transfusion. From this point onwards the rates of transfusion and exsanguination are kept equal as nearly as possible. If any clotting occurs a further 500 units of heparin is injected. When 400 ml. of blood has been withdrawn the radial artery is tied and the skin sutured. The remainder of the 500 ml. is allowed to run in, and the whole process is thus completed.

In an actual case the authors were able to demonstrate by differential agglutination tests that the expected degree of exchange did occur, approximately 90 per cent of cells in the final arterial sample being of the same type as the donor's.

[Whether or not the authors' thesis of damage by intravascular agglutination is correct, there are good reasons for wanting to effect a temporary replacement of Rh-positive by Rh-negative cells in the infant with icterus gravis. By supplying it with Rh-negative cells, which are not susceptible to rapid destruction, the stimulus to the bone marrow is reduced, less Rh-positive cells are produced and therefore less are destroyed. An exchange transfusion effects this process very rapidly and prevents loading of the infant's circulation with the products of blood destruction. Moreover, it must remove a large quantity of incomplete antibody from the infant's plasma. The authors' method has been found satisfactory in practice, and the only criticism is that cells in saline are injected; it would seem preferable to use heparinized whole blood for the transfusion, so as not to deplete the infant of plasma protein and so as to avoid the injection of a large amount of electrolyte, since if an ordinary bottle of stored blood is used for the transfusion the infant inevitably receives a large amount of citrate. Although the whole procedure is an attractive one, it is certainly more troublesome to perform than the ordinary drip transfusion and demands 2 to 3 hours of the operator's time. Only a large-scale follow-up of cases can show whether it brings any improvement in prognosis, particularly with regard to the late sequelae of the disease.]

P. L. Mollison

294. **The Encephalopathy (Kernicterus) of Erythroblastosis Fetalis, its Serologic Diagnosis and Pathogenesis.**

By A. S. Wiener and M. Brody. *Amer. J. ment. Defic.*, **51**, 1–14, July 1946. 3 figs., 34 refs.

A new theory is advanced to explain the occurrence of neurological signs and symptoms in jaundiced infants suffering from erythroblastosis foetalis. The condition, named kernicterus by Schmorl in 1903, is the result of areas of degeneration of ganglion cells, associated with demyelination, disseminated throughout the brain, usually but not necessarily revealed to the naked eye by bile-staining. The actual neurological picture depends on the extent and distribution of these areas, and may be extremely variable. It is claimed that the cerebral damage is the result of the formation of agglutination thrombi in capillaries of the brain, and that these are readily demonstrable in haematoxylin and eosin sections. Diamond, Blackfan, and Baty in 1932 demonstrated that congenital haemolytic anaemia, icterus gravis neonatorum, hydrops foetalis, and certain stillbirths all have a similar pathology, and suggested that

they are due to a common disease process. The discovery of the Rh factor by Landsteiner and Wiener in 1940 was soon followed by Levine's observations on iso-immunization in pregnancy and his theory of the causation of erythroblastosis. According to this theory, " an Rh-negative mother bearing an Rh-positive foetus may become sensitized to the Rh factor, and the Rh agglutinins thus produced may pass back through the placenta into the foetus, causing destruction of the blood of the foetus and giving rise to one or another manifestation of erythroblastosis ". A drawback to this hypothesis is that such agglutinins are demonstrable in less than half the proven cases of Rh-sensitivity, and no attempt is made to explain the variable clinical manifestations of erythroblastosis in different infants. About 10 per cent of all marriages involve Rh-negative women with Rh-positive husbands and children, yet only one in approximately 300 newborn infants is affected by erythroblastosis, presumably because only occasional Rh-negative women are readily sensitized to the Rh factor. Erythroblastosis can occur when the mother is Rh-positive, though the Rh factor accounts for 90 per cent of all cases. The other most common cause appears to be iso-immunization to the ordinary A-B blood group factors, although occasionally cases are shown to be due to variants of the Rh factor. The presence of sensitivity must be demonstrated by showing that abnormal antibodies (usually anti-Rh) are present in the mother's serum, as the mere demonstration that the mother is Rh-negative and the infant Rh-positive does not necessarily or usually indicate sensitivity.

A new type of antibody which does not produce agglutination of sensitized red cells was demonstrated in 1944 by Race and Wiener. These so-called blocking antibodies or glutinins are presumed to be univalent and to consist of smaller molecules than Rh agglutinins, which are probably bivalent in the chemical sense that each molecule has two specific combining groups for the corresponding antigen, and hence clumping of red cells takes place by the formation of a lattice-work. Blocking antibodies are able to combine with red cells in saline without producing any visible reaction, though in serum or plasma they can bring about clumping (conglutination) by the adsorption of X protein (conglutinin).

The authors believe that most of the cases of erythroblastosis complicated by neurological sequelae are due to the presence of agglutinins (bivalent antibodies) in the mother's serum, transferred to the foetal circulation during parturition, when the uterine activity " milks " them through the placenta. Because of their large molecular size these antibodies are not likely to traverse the placenta during pregnancy, and it is commonly found that these infants appear normal at birth, but soon become jaundiced and show signs of toxicity. The action of these antibodies is to cause agglutination of the infant's red cells in vessels where the circulation is slow, producing agglutination thrombi. The severe jaundice is the result of liver damage consequent on this pathological process, and involvement of bone marrow causes release of erythroblasts, often without any anaemia. Kernicterus is due to the same process in the brain. Occasionally the theory appears to break down by the occurrence of cases with only univalent Rh antibodies in the mother's serum, but it is believed that the development of X protein in the infant's serum (by dehydration or other mechanism) results in conglutination of the infant's red cells with sequelae indistinguishable from those of agglutination. Early and massive transference of univalent antibodies, which more readily traverse the placenta, results in a hydropic stillbirth because of the breakdown of " coated " red cells producing severe anaemia without agglutination. In milder cases the infant is born alive and can be saved by proper transfusion therapy with Rh-positive blood or the mother's washed red cells. This variety is ordinarily not complicated by kernicterus, but mixed pictures can occur due to the presence of both univalent and bivalent antibodies.

Alpha or beta antibodies developed in the maternal serum in response to A and B agglutinogens in the red cells of infants of an incompatible blood group may occasionally result in breakdown of their red cells and mild jaundice, often classified as physiological icterus. Occasionally severe or fatal instances of erythroblastosis may result from this mechanism, but this is exceptional because the placenta is relatively impermeable to natural alpha and beta agglutinins and the agglutinogens A and B are not well developed in infants' red cells.

Illustrative case histories with the results of serological examinations are described, one being a severe case of erythroblastosis due to sensitization to agglutinogen B, resulting in bilateral optic atrophy and complete idiocy. Pneumoencephalography revealed severe and widespread cerebral atrophy. It is emphasized that iso-immunization has not been demonstrated in Wilson's disease (3 cases) and that there is no relation between this condition and erythroblastosis. Early clamping of the umbilical cord is suggested to limit the transference of agglutinins from mother to child.

M. Baber

295. **The Rh Factor and its Importance in Medical Practice.** (Il fattore Rh e la sua importanza nella prassi medica.)
By F. DOMENICI. *Gazz. sanit. Milano.*, **17**, 137–140, Nov.–Dec. 1946.

296. **Role of the Rh Factor in Erythroblastosis.** (Rôle du facteur Rh dans l'érythroblastose du nouveau-né.)
By A. BERTRAND. *Union méd. Can.*, **75**, 1384–1390, Nov. 1946. 11 refs.

297. **Variation in the Titre of Rh Antibody during Pregnancy.**
By M. D. HICKEY and E. DE VALERA. *Brit. med. J.*, **1**, 335, March 15, 1947. 3 refs.

298. **The Rh Factor in Obstetrics.**
By E. JOOSTE. *S. Afr. med. J.*, **20**, 732–739, Dec. 14, 1946. 18 refs.

299. **The Rh Factor and Foetal Erythroblastosis.** (Factor Rh e eritoblastoses fetaes.)
By V. MONETTI. *Rev. Ginec. Obstet.*, **2**, 154–163, Sept. 1946. 24 refs.

300. **The Rh Factor and Erythroblastosis.**
By C. E. SNELLING. *Canad. med. Ass. J.*, **56**, 47–51, Jan. 1947. 28 refs.

301. **Mild Cases of Erythroblastosis Foetalis.** (Lichte gevallen van erythroblastosis foetalis.)
By S. I. de VRIES. *Ned. Tijdschr. Geneesk.*, **91**, 13–20, Jan. 4, 1947.

OBSTETRIC OPERATIONS

302. **Episiotomy.** (L'épisiotomie.)
By F. CHATILLON. *Rev. méd. Suisse rom.*, **66**, 777–782, Nov. 25, 1946.

303. **The Lower Segment Caesarean Operation.**
By J. RIDDELL. *Med. Pr.*, **217**, 71–75, Jan. 22, 1947. 3 figs.

304. **Advisability of Caesarean Section.** (Oportunidad de la cesárea vaginal.)
By R. RAMIREZ MERCHAN. *Med. Cirug.*, **10**, 433–436, Sept. 1946.

305. **Local Anesthesia for Cesarean Section.**
By F. P. LIGHT. *N. Y. St. J. Med.*, **47**, 48–52, Jan. 1, 1947. 3 figs., 1 ref.

GYNAECOLOGY

General

306. **Gynaecology in 1946.** (La gynécologie en 1946.)
By R. PALMER, *Paris méd.*, **36**, 561–564, Dec. 21, 1946.

307. **Essentials to Adequate Gynecologic Patient Study.**
By A. L. DIPPEL. *Tex. St. J. Med.*, **42**, 417–422, Nov. 1946.

308. **Frigidity: Aphrodisiac Effect of Testosterone Implantations.** (La frigidité; effets aphrodisiaques des implantations de testostérone.)
By I. BERNARD. *Gynécologie*, **43**, 201–209, Nov.–Dec. 1946.

Disorders of function

309. **Menstrual Insufficiency and its Treatment.** (Insuffisances menstruelles et leur traitement.)
By F. MORICARD. *Rev. franç. Gynéc.*, **42**, 20–28, Jan. 1947.

310. **Functional Dysmenorrhoea. Physiopathological Conception.** (Les dysménorrhées fonctionnelles. Conceptions physiopathologiques.)
By A. E. LIESSE. *Rev. franç. Gynéc.*, **42**, 29–38, Jan. 1947. 22 refs.

311. **The Climacteric—A Period of Endocrine Imbalance.**
By J. H. DARRAGH. *McGill med. J.*, **15**, 239–249, Oct. 1946. 12 refs.

312. **A Contribution to the Diagnosis of the Menopause.** (Een bijdrage tot de diagnostiek van het climacterium.)
By L. H. LEVIE. *Ned. Tijdschr. Geneesk.*, **91**, 204–206, Jan. 25, 1947.

313. **Value of Irradiation of the Pituitary Gland in Menopausal Disorders.** (Uber den Wert der Hypophysenbestrahlung bei klimakterischen Ausfallserscheinungen.)
By A. KOTEK. *Wien. klin. Wschr.*, **58**, 714–716, Nov. 29, 1946. 7 refs.

The results of irradiation of the pituitary gland

in 200 cases of menopausal disorder have been observed by the author over a period of at least 3 years at the Second University Clinic for Women's Diseases, Vienna. The disorders were mostly nervous, without evident anatomical lesions, and were partly due to an increase in adrenaline secretion (Högler test); hot flushes and palpitations were the most frequent complaints. The author found that all 200 patients complained of hot flushes, 102 of excessive sweating, about 60 of headache and dizziness and 3 of joint pains. Out of the 200, 25 had had a physiological menopause, 117 had been sterilized by X-rays, and 9 sterilized by operation; the remaining 49 had had a radical operation for carcinoma and prophylactic application of X-rays. No essential connexion was found between the origin of the menopause and the subsequent disorders. In treatment two exposures were given to the temporal region, a little above the middle of a line joining the lateral orbital margin with the external auditory meatus. The exposed fields had a diameter of 4 cm. Each dose measured 200 r at 180 kV. and 6 mA., at a skin distance of 30 cm., and with a filter of 0.4 mm. copper and 1 mm. aluminium. Steinhardt and a few others have recommended 4 to 5 applications, but recently, owing to the danger of skin lesions, attempts to obtain better results with more than 2 exposures have been abandoned.

Results of treatment were classified under 3 headings: (1) age of patient; (2) original cause of the menopausal disorder; (3) time elapsed before beginning irradiation.

TABLE I

	Total number of patients	Patients under 40 years	Patients aged 41–45 years	Patients aged 46–50 years	Patients over 50 years of age
Cured ..	21	4 (11%)	6 (10%)	6 (8%)	5 (14%)
Improved	104	17 (48%)	31 (54%)	38 (51%)	18 (53%)
Not improved	75	14 (41%)	20 (36%)	30 (41%)	11 (33%)

Table I shows no connexion between results and any specific age. Four women under 40, all patients who had been treated by the radical operation for carcinoma of the cervix and later given X-ray therapy, showed the best results from X-ray treatment of the pituitary. This finding was general among patients who had received such treatment for carcinoma as is shown in Table II.

TABLE II

	Physiological Menopause	Surgical Sterilization	X-ray Sterilization	Carcinomata	Total
Cured ..	—	—	14 (12%)	7 (14%)	21 (10.5%)
Improved	13 (52%)	5 (55%)	61 (52%)	25 (51%)	104 (52%)
Not improved	12 (48%)	4 (45%)	42 (36%)	17 (35%)	75 (37.5%)

Better results were obtained when the lower abdomen had been irradiated, as in X-ray sterilization or post-operative irradiation given for carcinoma. This observation has also been made by Steinhardt, but no explanation of it is known. There was no essential difference in the percentage results when classified by lapse of time since the menopause. Among the 200 cases were 6 women who reported no improvement after pituitary irradiation, but spontaneous improvement 2 to 7 years later.

Summarizing the results, the author states that 10.5 per cent of 200 patients were permanently cured; this contrasts with the figures of Borak, Porchownik, and Steinhardt, which were much higher. In the 104 (52 per cent) patients who showed improvement, 50 have been irradiated 2 or 3 times at intervals of 2 to 15 months, owing to recurrence of their symptoms. If after 3 periods only slight improvement had taken place no further irradiation was given, in view of the danger of local skin lesions. After the second irradiation an interval of 6 to 12 months had to be allowed. The improvement lasted twice as long after the second irradiation as after the first; this excludes a psychological factor. Considering that 75 in 200 cases (37.5 per cent) were absolute failures, this treatment can scarcely be recommended and has been discontinued at the Vienna University Clinic.

M. Schieber

314. **The Treatment of Benign Menopausal Bleeding.**
By J. R. WILLSON. *J. Kansas med. Soc.*, **47**, 493–495, Nov. 1946. 3 refs.

315. **Treatment of Leucorrhoea.** (Tratamiento del flujo genital.)
By A. A. PUNTEL and E. A. PIZARRO. *Rev. Med. Cien. af.*, **8**, 886–893, Nov. 1946.

316. **Sterility.** (Stérilité.)
By F. X. DEMERS. *Union méd. Can.*, **75**, 1462–1468, Nov. 1946.

317. **The Decline in Fertility.**
By P. H. J. TURTON. *Med. Offr.*, **76**, 249–250, Dec. 7, 1946.

The author deals with the social consequences of a decline in fertility. For more than 60 years the birth-rate of England and Wales has declined while the population has increased. During this period there was a rise of 68 per cent in those aged 65 years and over, and a decrease of 14.4 per cent in those under 25. In the future, simultaneously with the raising of the school-leaving age to 16 years and the maintenance of conscription, the number of old-age pensioners will go up steadily to a figure representing 31 per cent of the total population in 1961, so that it will be difficult to find the workers to carry this load of passengers. A chart gives the age distribution of population for England and Wales. The author, quoting extensively from the criticism of Joad and Desmond MacCarthy by Harrod in the *Economic Journal*, states that " . . . unless a rather spectacular increase in the size of families occurs in the decades immediately ahead, the decline of population will not be arrested in the twentieth century. . . . Those who wish to arrest the decline are charged with seeking cannon fodder. . . . In Britain such an argument, whatever truth it may have had in the past, is now obsolete."

Discussing the problems of the aged, the author remarks that the aged and infirm cannot be discarded as so much worn-out junk fit only for the scrapheap. An increase in number of hospital beds for the senile and chronic sick is useless without additional staff. Not only is the problem of the chronic sick not being met, but most people do not realise that there is a problem. The present insufficient accommodation is often in grim, depressing, ill-cared-for institutions. As by 1950 there will be over 5,000,000 people over 65 years of age, the need for more and better beds for old people is urgent. The author ends his critical survey by expressing the opinion that many trained personnel are being wasted. Industrial firms engage the services of registered nurses to act as dressers and attendants in first-aid rooms; to a large extent the services of these could be more usefully employed where the need is more urgent. [Many would consider it more important for a nation to maintain the health of the active worker than to relieve the old and infirm.] *A. Michael Critchley.*

318. **A Case of Sterility.**
By E. JACOBSON. *Psychoanal. Quart.*, **25**, 330–350, July 1946. 5 refs.

The case of a married woman of 35 is described. She had started to menstruate at 14 and up to 16 had developed rapidly and menstruated very freely. She worried about her obesity, dieted, worked too hard, lost weight rapidly, and became amenorrhoeic. She was so markedly of the glandular dysfunction type that her condition was diagnosed as Simmonds's disease. She married at 24 in spite of her amenorrhoea. She improved on oestrin and menstruated a few times, but did not become pregnant. She adopted a child, but this was not a success, and it was only when she came for analytical treatment that she began to improve. She gained weight and after 6 months desired to adopt another child, but in the eighth month of treatment became pregnant and was delivered of a healthy girl. Although analysis was not complete the patient was so happy that she broke off treatment, though she returned later for intermittent help. She came of a poverty-stricken Jewish family with a gentle father and very domineering mother. In prepuberty she had gone through a phase of over-submissiveness and then one of extreme aggression. This was followed by a stormy love affair with a Gentile boy, which filled her with deep guilt feelings; later she married a Jew. Dreams illustrative of her strong ambivalent feelings towards her parents and siblings are narrated. In this case there was violent regression to pregenital oral and anal levels with some constitutional factors. The feature of the case is the amazing glandular changes which were apparently psychically determined and the extraordinary change induced by analysis. She became pregnant twice more but underwent abortions. For a time she wished to submit to artificial sterilization; although she abandoned this project she again became amenorrhoeic, which made her very happy and solved her problems. As the author remarks, the neurosis had the last word.

R. G. Gordon

319. **A Review of the Present Position of the Investigation of Sterility and Infertility in the Female.**
By C. B. MURLESS. *S. Afr. med. J.*, **20**, 788–793, Dec. 28, 1946. 13 refs.

320. **Evaluation of the Male Factor in Conjugal Sterility.** (Evaluation du facteur masculin dans la stérilité conjugale.)

By R. PALMER and G. GUILLON. *Rev. franç. Gynéc.*, **42**, 1–19, Jan. 1947. 23 figs., 14 refs.

Abnormalities of the reproductive organs

321. **A Case of Pseudohermaphroditism Treated by Surgery and Hormones.** (Un cas de pseudohermaphrodisme, traité par la voie chiruogicale et hormonale.)

By M. R. TACHEZY. *Scapel. Brux.*, **99**, 722–725, Nov. 30, 1946. 9 figs.

322. **Vulvar and Vaginal Dystrophy; Kraurosis Vulvae.** (De la dystrophie vulvaire et vaginal dite "Kraurosis vulvae".)

By P. MOULONGUET. *Paris méd.*, **36**, 564–567. Dec. 21, 1946.

323. **Severe Cases of Stenosis of the Female Urethra.** (Uber hochgradige Stenosen der weiblichen Urethra.)

By G. TZAMALOUKAS. *Klin. med., Wien.*, **1**, 553–556, Nov. 1, 1946. 17 refs.

324. **Uretero-vaginal Fistula.** (A propos de fistule urétéro-vaginale.)

By P. BOURGEOIS and R. SIMARD. *Union méd. Can.*, **75**, 1645–1647. Dec. 1946.

Infections of the reproductive organs

325. **The Importance of the pH in the Treatment of Diseases of the Vagina.**

By C. A. ANDERSON. *North Carolina med. J.*, **8**, 29–31, Jan. 1947. 1 ref.

326. **Results Obtained with Penicillin Treatment of Gonorrhoea.** (Ergebnis der Tripperbehandlung mit Penicillin.)

By K. HOEDE, E. BAYER, and K. D. EBBINGHAUS. *Med. Klinik.*, **41**, 443–446, Oct. 1946. 1 ref.

New growths of the reproductive organs.

327. **Epithelial Changes in the Uterine Glands in Glandular-Cystic Hyperplasia.** (Uber eigentümliche Epithelveränderungen an den Uterindrüsen bei glandulärzystischer Hyperplasie.)

By I. OBIDITSCH-MAYER. *Klin. Med., Wien.*, **1**, 500–505, Oct. 1, 1946. 4 figs., 10 refs.

The author found some large cells, which he likens to Hamperl's "onkocytes", in the glands of a hyperplastic endometrium. [The grounds for such a comparison are dubious, even if one accepts Hamperl's ideas about "onkocytes".]

R. A. Willis

328. **Tumours of the Female Genital Tract.**

By R. W. Te LINDE. *Bull. N. Y. Acad. Med.*, **23**, 10–19, Jan. 1947.

329. **A Cancer Control Project in a Planned Parenthood Center.**

By E. V. BERG. *Hum. Fertil.*, **2**, 75–78, Sept. 1946.

The author's work was inspired by a report by MacFarlane and others which appeared in January 1942, in the *Pennsylvania Medical Journal*. This report described an attempt to control cancer of the uterus by pelvic examination twice a year of volunteers, ranging in age from 30 to 80. In the first 1,000 individuals examined, 4 cases of cancer were found and 471 benign lesions, of which 291 were considered to be "precancerous lesions of the cervix". The author describes a similar scheme applied to women attending the Nassau-Suffolk Planned Parenthood Center and the findings in the first 1,000 patients. They were all married women. No case of cancer was discovered, but 525 of the patients had local disease which justified reference to their own physician. The lesions discovered are analysed in a table. Only 39 of the 525 had had previous treatment or were at the time under treatment for these conditions. A further 319 received treatment after their first visit to the Center, and a table is included of the types of treatment carried out. [It would be interesting to know what happened to 167 of the 525, for it is not recorded that they received treatment.] The advantages of the scheme in relation to such a centre are discussed.

R. H. Parry

330. **Vaginal Cell Examination as a Routine in Diagnosis. A Study of Vaginal and Cervical Cytology as Related to Abnormal Growths.**

By J. E. AYRE. *Sth. med. J.*, **39**, 847–852, Nov. 1946. 6 figs., 13 refs.

Cytological studies were made on 2,320 patients for the diagnosis of gynaecological cancer; 226 reports were "positive", and of these 202 were confirmed by biopsy. The error rate of a negative diagnosis proved to be 4.8 per cent, and of a positive one 1.13 per cent. The author has followed on the pioneer work of Papanicolaou, but has altered the latter's technique by taking suction specimens of the squamo-columnar junction of the cervical canal. The underlying principle of the study is that the epithelium derived from the Müllerian tract possesses the characteristic of desquamation, and that the cells so thrown off pass in the physiological stream down the uterus, tubes, and vagina. Most malignant lesions here are exfoliative, and hence they too tend to desquamate.

Besides the provision of easy and rapid diagnosis of evident cancer the author is convinced that this technique will be of great help in diagnosing cases in a clinically " pre-cancerous " condition, and thus enable operation or other treatment to be carried out much earlier.

The signs considered diagnostic of a pre-cancerous condition are the presence of anaplastic squamous cells, an abnormally high degree of cornification in the cells, multinucleation of these cells, and the finding of atypical cornified cells with dense pyknotic nuclei. In the series 19 such cases were identified. These conformed to Novak's description of the pre-cancerous state as lesions which exhibit cell activity unusual in benign conditions and yet lack certain characteristics of actual cancer. An easy method of carrying out this form of biopsy and keeping the specimens fresh for postal transmission is described. The smear is fixed in ether and alcohol for an hour, and then a small quantity of glycerin is put on it and the slide is covered by another. The individuals diagnosed as pre-cancerous were also submitted to investigations of thiamine and oestrogen activity; they showed high endogenous oestrogen levels with a thiamine deficiency. Similar changes were observed in 50 cases of proved cancer, but not in 50 control cases of benign lesions. The possibility of the existence of a metabolic factor in uterine cancer is therefore raised. The smear technique has obviously also application to most conditions in the genital tract.

Kenneth Bowes

331. **Haemoperitoneum due to Ectopic Chorion-epithelioma.** (Emoperitoneo da corioepitelioma ectopico.)

By F. MATTEACE. *Clin. oster. ginec.*, **48**, 180–191, Sept.–Oct. 1946. 19 refs.

The author records a case in which death from haemoperitoneum occurred 18 months after the expulsion of a vesicular mole. There had been two negative laparotomies. The Friedmann reaction had been weakly positive throughout. Only at necropsy was the diagnosis made of chorion-epithelioma arising retroperitoneally near the bifurcation of the common iliac artery. The author reviews the literature and discusses the pathology and clinical features, concluding that many cases of chorionepithelioma are, like the one described, difficult to diagnose.

A. S. Bullough

332. **Recurring Hematocolpometra Associated with Carcinoma Treated by Partial Hysterectomy: Report of Case.**

By L. C. HALLENDORF and W. R. LOVELACE. *Proc. Mayo Clin.*, **22**, 38–40, Jan. 22, 1947. 4 refs.

333. **Solid Tumour of the Vulva.** (Tumor solido da vulva.)

By A. R. de OLIVEIRA MOTTA. *Rev. Ginec. Obstet.*, **2**, 273–277, Nov. 1946. 3 figs.

334. **Twenty Cases of Carcinoma of the Cervix Uteri Treated by Radiosurgery. (Gosset-Wallon Technique.)** (Une série de vingt cancers du col utérin traités par l'association radium-chirurgie [technique de Gosset-Wallon].)

By J. LANGE. *Bordeaux. chir.*, 14–20, Jan.–Apr., 1947.

335. **Rhabdomyosarcoma of the Cervix and Vagina in a 7 months old Infant.** (Uber ein rhabdomyomatöses Traubensarkom der Cervix und Vagina bei einem 7 Monate alten Kind.)

By W. KOHLMEIER. *Klin. Med.*, **1**, 571–577, Dec. 1, 1946. 3 figs., 6 refs.

336. **Fibromyoma of the Uterine Cervix.** (Contribution à l'étude du fibromyome du col utérin.)

By —. BOURG and —. HANNES. *Brux. méd.*, **27**, 577–583, Mar. 16, 1947. 1 fig., 25 refs.

337. **Endophytic Carcinoma of the Cervix Uteri with " Portio Lacunaris ".** (Ein endophytisches Kollumkarzinom mit einer " Portio lacunaris ".)

By V. GRUNBERGER. *Krebsarzt*, **1**, 522–528, Dec. 1946. 3 figs., 5 refs.

338. **Metastasis of Carcinoma of the Cervix Uteri Adnexa.** (Zur Kenntnis der Metastasierung des Kollumkarzinoms in die Adnexa.)

By O. SCHINKELE. *Klin. med.*, **1**, 595–601, Dec. 1, 1946. 4 figs., 13 refs.

339. **Cervical Stump Carcinoma after Subtotal Hysterectomy.** (Cancérisation du moignon du col utérin après hystérectomie subtotale.)

By G. SAINT-ARNAUD. *Laval méd.*, **11**, 906–910, Nov. 1946. 7 refs.

340. **Calcareous Tumours of the Uterus.** (Tumores calcareos uterinos.)

By E. St. LOOP. *Obstet. Ginec. lat.-amer.*, **4**, 836–841, Nov. 1946. 2 figs., 5 refs.

341. **Independent Treatment of a Malignant Tumour of the Uterus in Labour.** (Przypadek samoistnego wyleczenia zamartwiczego miesniaka macicy w pologu.)

By J. DOLINSKY. *Polsk. Tyg. lek.*, **1**, 1125–1127, Sept. 16, 1946.

342. **A Case of Combined Subserous Pedunculated Fibroma and Sarcoma of the Uterus.** (Su di un caso di associazione neoplastica dell'aparato genitale feminile.

[Fibroma peduncolato sottosieroso e leiosarcoma dell' utero].)

By L. de BELLIS. *Clin. Ostet. Ginec.*, **48**, 246–253, Nov.–Dec. 1946. 2 figs., 17 refs.

343. **A Case of Endometriosis Ilei.** (Et Tilfaelde af Endometriose i Ileum.)

By T. POULSEN. *Nord. Med.*, **33**, 63–64, Jan. 10, 1947. 1 fig., 3 refs.

344. **Adenomyosis of the Uterus. A study of 52 Reported Cases and a Review of the Literature.**

By S. D. SPATT. *Amer. J. Obstet. Gynec.*, **52**, 581–587, Oct. 1946. 39 refs.

The author presents 52 cases of uterine adenomyosis in which the endometrium has been carefully studied. He correlates his findings with those of others in a review of the literature. Endometrial findings are probably of the greatest value at the present time in the study of abnormalities of ovarian secretion, owing to the difficulty of obtaining accurate direct hormone titres. Varying figures are given by different authors for the incidence of adenomyosis, but it is concluded that it occurs in 5 to 10 per cent of myomatous uteri. The highest number of cases occur between the ages of 40 and 50. Symptoms in the present series were "metromenorrhagia" in 56 per cent, dysmenorrhoea in 29 per cent, both together in 17 per cent, and backache in 3 per cent, but in no case was adenomyosis present alone. The endometrium was studied in 50 out of the 52 cases and the anovulatory cycle was found to be present in 31. It is suggested that over-production of oestrogen may be a common factor in causing the endometrial changes and the adenomyosis. Fibroids and adenomyosis are also frequently associated, suggesting a common aetiology. Pelvic inflammation and ovarian cysts were also frequently found. *Josephine Barnes*

345. **Angiomyomatosis of Uterus.** (Angiomyomatose de l'utérus.)

By J. P. DAVEO and J. MORISSON-LACOMBE. *Rev. franç. Gynéc.*, **41**, 352–355, Nov. 1946. 1 fig., 4 refs.

346. **Dysgerminoma of the Ovary.**

By W. C. CUSTER. *Surgery*, **20**, 520–524, Oct. 1946. 3 figs., 4 refs.

Dysgerminoma of the ovary arises from undifferentiated sex cells of the primitive mesenchyme and tends to occur in young subjects whose secondary sex characteristics may be abnormal. Its incidence among malignant ovarian tumours is variously given as between 3 and 6 per cent. The presenting symptom in these cases is usually abdominal distension, pain and menstrual irregularities being rare. Sex hormone studies are of no value in diagnosis, which is usually made at operation. The tumour must always be regarded as malignant and treated by operative removal. X-ray irradiation is without effect.

A case is reported in a 12-year-old girl in whom the presence of an abdominal mass had been found at a routine examination. The mass extended from the left side of the pelvis to above the umbilicus, was irregular and mobile and not tender on palpation. Pelvic examination did not allow of its differentiation from the uterus. Laparotomy disclosed a large mass, weighing over a kilogramme and replacing the left ovary, firm, discrete, and non-adherent to surrounding structures. The surface was opaque, pale grey, and fairly smooth. On section, patches of haemorrhage and degeneration were seen, but no cystic areas. Histologically, the tumour consisted of cords and nests of large cells with pale cytoplasm and large vesicular nuclei, often with atypical mitotic figures, and with a variable amount of fibrous stroma.

A follow-up examination of the child 18 months later revealed no evidence of recurrence or metastasis. *S. S. B. Gilder*

347. **Gonocytoma. Homologous Ovarian and Testicular Tumours. I. With Discussion of "Mesonephroma Ovarii."** [In English.]

By G. TEILUM. *Acta path microbiol. scand.*, **23**, 242–251. 1946. 13 figs., 14 refs.

The author applies the term "gonocytoma" to a series of similar tumours which occur in the ovary and the testis. In the testis the tumours derive from early stages of the germ cells, and in the ovary from the homologous cells in the remnants of the medullary cords. The normal disappearance of these cells from the ovary explains the lower frequency of the tumours in women, their restriction to lower age groups, and the frequent coexistence of developmental abnormalities of the genital organs. Three subdivisions are recognised in testis and ovary. Gonocytoma I corresponds with seminoma in the testis and with dysgerminoma in the ovary; it does not produce chorionic gonadotrophin. Gonocytoma III corresponds with chorionepithelioma in both testis and ovary and

secretes chorionic gonadotrophin. Gonocytoma II, with which this paper is particularly concerned, is an " intermediate form ", both histologically, and in the irregular secretion of gonadotrophin.

Teilum describes 4 malignant, radio-resistant tumours of the testis in men ranging from 26 to 40 years of age. Histologically the tumours were most often adenopapilliferous; they were either solid or cystic and sometimes teratoid, and transitions were traced on the one hand to undifferentiated seminoma and on the other to chorionepithelioma. He makes a detailed comparison of these tumours with ovarian tumours variously described and called mesonephroma ovarii by Schiller (*Amer. J. Cancer*, 1939, **35**, 1), and concludes that the testicular and ovarian tumours are similar in structure and origin, both belonging to the " intermediate form ", Gonocytoma II. He contrasts with Schiller's tumours a malignant ovarian tumour in a woman aged 45; this tumour he considers to be a true mesonephroma.

L. Foulds.

348. **Arrhenoblastoma—Androblastoma. Homologous Ovarian and Testicular Tumours. II. Including the so-called " Luteomas " and " Adrenal Tumours " of the Ovary and the Interstitial Cell Tumours of the Testis.** [In English.]

By G. TEILUM. *Acta path. microbiol. scand.*, **23**, 252–263, 1946, 23 figs., 30 refs.

In addition to the gonocyctoma (see Abstract No. 347) the author recognises a second series of homologous tumours occurring in both ovary and testis—namely, the arrhenoblastoma or androblastoma series. Robert Meyer derived the arrhenoblastoma of the ovary from testicular elements remaining from early stages of gonadogenesis. On this hypothesis similar tumours would be expected in the testis, but none has been described hitherto. Teilum now describes such a testicular tumour removed from a man aged 53. The left testis had been enlarged for 30 years, but had increased in size during the last 2 years; impotence had been present for 3 years, and gynaecomastia for 1 year. The gynaecomastia subsided partially after removal of the enlarged tesis. The histological picture was very varied, but transitional forms showed that the diverse structures represented different stages of differentiation of a single blastoma. All the characteristic histological features of ovarian arrhenoblastoma were present. Further, gradual transitions were demonstrated from tumour tissue of androblastoma type to clear-cut " lipoid cell tumour ". This tissue was histologically identical with that of the lipoid-containing ovarian tumours which, though usually described as " luteoma ", " adrenal tumour ", " ovarian hypernephroma ", or " folliculome lipidique ", should now be regarded as particularly lipoidal forms of ovarian arrhenoblastoma. Other variants show a more or less pronounced differentiation in the direction of testicular interstitial-cell tumour and a homologous " extra-glandular " interstitial-cell tumour of the ovary. The androblastoma (arrhenoblastoma) series represents a later developmental stage than the gonocytoma and shows differentiation in greater or less degree towards normal testicular elements. The fact that the tumours are virilizing in women and feminizing in men does not, in Teilum's opinion, disprove their homology, for this paradoxical effect is commonly shown by adrenal tumours; probably chemically related steroid substances with oestrogenic or androgenic activity are present in addition to the normal sex hormones.

L. Foulds

349. **Gangrenous Ovarian Cyst in a Child of Four, and Rupture of the Heart.**

By E. R. SELBY. *Canad. med. Ass. J.*, **56**, 74–75, Jan. 1947.

350. **A Case of Psammocarcinoma of the Ovaries Developing After 18 Years.** (Un cas de psammo-carcinome des ovaires qui évolue depuis 18 ans.)

By R. SARASIN. *Gastroenterologia, Basel*, **71**, 315–321, 1946. 3 figs.

351. **Cystic Teratoma of the Ovary Infected with *Erbethella typhi*.** (Teratoma quístico del ovario, infectado por bacilos de Eberth.)

By A. DURAN BUENDIA and S. FUENZALIDA. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 141–143, Sept. 1946.

352. **Tumours of the Ovarian Parenchyma.** (Les tumeurs du parenchyme ovarien.)

By A. CORNIL. *Acta chir. belge.*, **45**, 363–394, Dec. 1946. 7 figs., bibliography.

353. **Co-existent Primary Carcinoma of the Fallopian Tube and of the Breast. Report of a Case.**

By J. F. CURRAN and E. A. KILROY. *New. Engl. J. Med.*, **236**, 64–65, Jan. 9, 1947. 4 refs.

Operations

354. **Observations on Hysterectomy.**

By J. K. FEENEY. *Irish J. med. Sci.*, 6th series, 1–13, Jan. 1947.

This is a detailed review of 508 hysterectomies (3 Wertheim, 275 abdominal total, 105 abdominal sub-total, and 125 vaginal) performed by the author and Prof. J. F. Cunningham in St. Vincent's Hospital, Dublin, and in nursing-homes. It covers in detail the various indications for and the advantages and disadvantages of the 4 types of operation. The overall mortality rate was 0.59 per cent. Major accidents, complications, and post-operative morbidity are discussed. Of 19 patients with carcinoma of the body of the uterus 18 were treated by abdominal total hysterectomy and 1 (with procidentia) by vaginal hysterectomy. Two are alive and well after 5 years, 4 after 3 years, 3 after 2 years, 1 after 18 months, and 1 after 6 months. Eight died of a recurrence of the growth within periods varying from 4 to 16 months. There was 1 death in operation.

A considerable part of the paper is devoted to a description of pre-operative preparation for abdominal hysterectomy and the technique of the operation of abdominal total hysterectomy. On 40 occasions vaginal hysterectomy was performed under local analgesia, using 1 per cent " novutox " after morphine-scopolamine sedation. There are no references.

[The technique of local infiltration for vaginal hysterectomy is not discussed. There is no indication whether the operators have abandoned this method of analgesia (40 out of 125 cases) or not. No mention is made of inversion of the vagina following abdominal total hysterectomy. As the operators do not stitch the round-ligament stumps to the vaginal angles, it would have been interesting to record whether inversion occurred or not.]

G. Gordon Lennon

355. **A Report of 2,798 Vaginal Hysterectomies.** By Z. B. CAMPBELL. *Amer. J. Obstet. Gynec.*, **52**, 598–613, Oct. 1946. 27 refs.

This is a discussion of 2,798 vaginal hysterectomies for benign disease of the uterus. The operation is frequently combined with colpoperineorrhaphy, and the advantages of this are stressed. The author believes that the uterus should be removed by the vaginal route whenever possible. Advantages of the vaginal route are the absence of an abdominal incision and the decreased risk of pulmonary complications of thrombophlebitis, and of bowel complications. Post-operative discomfort is also less than after abdominal hysterectomy. There is no reason why the vagina should become shorter after vaginal than after abdominal hysterectomy, since the opening into it is made at the same level. Vaginal hysterectomy has been recommended for patients who are poor operative risks, but it seems logical to consider it an even safer procedure than abdominal hysterectomy in patients who are good risks. No definite contra-indications can be laid down, but conditions which obviously make the vaginal route more risky than the abdominal would in general lead to the choice of the latter method. Pre-operative preparation is important and should be directed to clearing up foci of infection, both local and remote, and to correction of anaemia, vitamin deficiency, and poor general nutrition.

The morbidity rate for the whole series, taking as the standard a temperature of over 100.4°F. (38°C.) on any two consecutive days, excluding the first 24 hours, was 36.5 per cent. Causes of morbidity included urinary tract infections, post-operative haematomata, and local infections. The bladder was opened on a number of occasions, and primary suture was performed; vesico-vaginal fistula resulted in 5 cases, and all were eventually cured. Recto-vaginal fistula occurred in 1 case. Prolapse of the Fallopian tube was fairly common; this complication can be dealt with easily by ligating the prolapsed tube and burning it off with the nasal cautery. The average stay in hospital did not exceed 13.5 days. Six patients died (0.214 per cent). This compares very favourably with results as given by other authors. In the summary the need for meticulous haemostasis is again emphasized. *Josephine Barnes*

356. **Hysterectomy. A Study of 607 Cases.** By C. H. TYRONE, C. G. COLLINS, J. C. WEED, R. F. ZEIGLER, and J. B. CRAWFORD. *Sth. med. J.*, **39**, 957–960, Dec. 1946. 2 figs.

357. **Post-operative Cervical Elongation.** (Elongaciones cervicales postoperatorias.) By N. O. DI FONZO. *Rev. méd.-quirúrg. Pat. fem.*, **25**, 416–418, Sept. 1946.

358. **Accidental Vascular Injection during Hysterosalpingography.** (Inyeccion vascular accidental durante la histerosalpingografia.) By A. PIERNES, F. IBARROLA, and E. ROSSELLI. *Rev. med.-quirúrg. Pat. fem.*, **25**, 411–415, Sept. 1946. 2 figs.

359. **Vaginal Aplasia. Formation of a New Vagina by McIndoe's Technique.** (Aplasia vaginal. Formación de una neovagina con la técnica de McIndoe.)

By C. A. Brea and R. C. O'Connor. *Prensa med. argent.*, **33**, 2494–2500, Dec. 13, 1946. 7 figs.

360. **Modified Sturmdorf Suture.** (Modifizierte Sturmdorfnaht.)

By A. H. Palmrich. *Klin. med.*, **1**, 601–604, Dec. 1, 1946. 4 figs.

361. **The Modern Technic of the Le Fort Operation.**

By R. Tauber. *Ann. Surg.*, **125**, 334–340, Mar. 1947. 3 figs., 44 refs.

See also Nos. 321, 332, 334, 339

Urology

362. **Urology in Women.** (Contribución al estudio de la urología en la mujer.)

By J. Falconi Mejia. *Rev. méd. peruana*, **19**, 247–304, May 1946.

363. **The Problem of Stress Incontinence and its Surgical Relief.**

By W. E. Studdiford. *Surg. Gynec. Obstet.*, **83**, 742–750, Dec. 1946. 9 figs., 20 refs.

The problems here considered are the surgical relief of patients when a previous operation for stress incontinence has failed and the avoidance of such failures. Forty-four cases have been operated on by the technique here described, of which 13 have already been reported. They include a case of congenital urethrocele and one occurring in a nulliparous patient of 70 years of age, the remainder being the more or less remote effects of childbirth. A review of available labour records revealed that in a surprisingly large number delivery had taken place without obvious injury; it is suggested that efforts to preserve the perineum may result in forward projection of the presenting part and consequent injury to the urethral attachments.

The operation here described and advocated (with admirable illustrations) is a modification of the Aldridge technique, in which a strip of rectus fascia is used to reinforce the pubo-cervical fascia supporting the urethra. In this operation a strip of rectus fascia is used in such a way as to form a sling supporting the urethra; both ends of the strip are fixed just above the symphysis. The operation is done in two stages with one change in position. *Stage I* is performed with the patient in the lithotomy position. Details are given of each step of the operation; as in the operative repair of cystocele, vaginal flaps are formed extending to the base of the urethra, and the pubo-cervical fascia is divided in the line of the vaginal incision; flaps of this fascia about 2 cm. wide are formed on each side. The plane between the vaginal flap and the fascial flap on each side is dissected up by the finger and extended upward, behind and to each side of the symphysis. The lateral fascial attachment is ruptured by the finger, which then enters the space of Retzius lateral to the bladder neck. There is some venous bleeding during this blunt dissection; it is said to be easily controlled by pressure. At this point the pubo-cervical fascial flaps are approximated by mattress sutures in such a way as to elevate the bladder neck behind the symphysis. When the line of sutures is completed, one end of a rubber tube (Penrose drain), about 30 cm. long, is placed in the space of Retzius on the left side, the other end being pushed by means of forceps into the corresponding space on the right side. The vaginal flaps are now trimmed and closed by a line of sutures, care being taken to avoid the underlying Penrose drain. For *Stage II* the patient is placed in the dorsal position. A midline incision is made from the symphysis to just above the umbilicus and a strip of rectus fascia, with its attached base below and to the left, is formed corresponding in length to the abdominal incision. Care must be taken at the levels of tendinous intersection so that the strip is not weakened during the dissection. The bladder is freed from the upper aspect of the symphysis, and the ends of the Penrose drain are located. The free end of the strip is fixed by suture to the left end of the drain and the strip is drawn through by traction on the other end of the drain. The strip is fixed to the right rectus sheath by a few sutures, care being taken that the sling so formed is not drawn too tight. The abdominal wound is then closed in layers. Generally it is not necessary to open the peritoneum. Post-operatively sulphadizine 0.5 g. is given 4 times a day until the catheter is removed. This is generally done on the ninth day, but normal urination is often delayed and the catheter may have to be re-inserted. In spite of a few failures, the results are regarded as satisfactory, especially in view of the fact that many of the cases had been previously operated upon.

T. C. Claire